



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>A61B 17/32</b>		A1	(11) International Publication Number: <b>WO 97/42888</b> (43) International Publication Date: 20 November 1997 (20.11.97)																					
<p>(21) International Application Number: <b>PCT/US97/08762</b></p> <p>(22) International Filing Date: <b>16 May 1997 (16.05.97)</b></p> <p>(30) Priority Data:</p> <table> <tr><td>60/017,133</td><td>17 May 1996 (17.05.96)</td><td>US</td></tr> <tr><td>60/019,918</td><td>14 June 1996 (14.06.96)</td><td>US</td></tr> <tr><td>60/023,658</td><td>1 August 1996 (01.08.96)</td><td>US</td></tr> <tr><td>60/025,340</td><td>3 September 1996 (03.09.96)</td><td>US</td></tr> <tr><td>08/714,548</td><td>16 September 1996 (16.09.96)</td><td>US</td></tr> <tr><td>08/710,456</td><td>17 September 1996 (17.09.96)</td><td>US</td></tr> <tr><td>08/727,074</td><td>8 October 1996 (08.10.96)</td><td>US</td></tr> </table> <p>(71) Applicant (<i>for all designated States except US</i>): <b>MERCURY DIAGNOSTICS INC. [US/US]; Suite D, 1137 San Antonio Road, Palo Alto, CA 94303 (US).</b></p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (<i>for US only</i>): <b>DOUGLAS, Joel, S. [US/US]; 2048 Calabazas Boulevard, Santa Clara, CA 95051 (US). ROE, Jeffrey, N. [US/US]; 3212 Veracruz Drive, San Ramon, CA 94583 (US). RADWANSKI, Ryszard [US/US]; 7003 "G" Rodling Street, San Jose, CA 95138 (US). GRAGE, Henry, M., Jr. [US/US]; 175 Tenby Terrace, Danville, CA 94506 (US). SANCHEZ, Michael, S. [US/US]; 682 Rustic Lane, Mountain View, CA 94040</b></p>		60/017,133	17 May 1996 (17.05.96)	US	60/019,918	14 June 1996 (14.06.96)	US	60/023,658	1 August 1996 (01.08.96)	US	60/025,340	3 September 1996 (03.09.96)	US	08/714,548	16 September 1996 (16.09.96)	US	08/710,456	17 September 1996 (17.09.96)	US	08/727,074	8 October 1996 (08.10.96)	US	<p>(US). DREXLER, Andrew, M. [US/US]; 12580 La Cresta Drive, Los Altos Hills, CA 94022 (US). DUCHON, Brent, G. [US/US]; 410 Milan Drive #106, San Jose, CA 95134 (US).</p> <p>(74) Agents: <b>DILLAHUNTY, T., Gene et al.; Burns, Doane, Swecker &amp; Mathis, L.L.P., P.O. Box 1404, Alexandria, VA 22313-1404 (US).</b></p> <p>(81) Designated States: <b>AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</b></p> <p><b>Published</b>  <i>With international search report.</i>  <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>	
60/017,133	17 May 1996 (17.05.96)	US																						
60/019,918	14 June 1996 (14.06.96)	US																						
60/023,658	1 August 1996 (01.08.96)	US																						
60/025,340	3 September 1996 (03.09.96)	US																						
08/714,548	16 September 1996 (16.09.96)	US																						
08/710,456	17 September 1996 (17.09.96)	US																						
08/727,074	8 October 1996 (08.10.96)	US																						
<p>(54) Title: <b>BLOOD AND INTERSTITIAL FLUID SAMPLING DEVICE</b></p> <p>(57) Abstract</p> <p>A device and method for lancing a patient, virtually simultaneously producing and collecting a small fluid sample from a body. The device comprises a blood collection system including a lancing needle (16), drive mechanism (11), kneading or vibration mechanism (25), optional suction system (7), and sample ejection mechanism. The device is preferably sized to be hand-held in one hand and operable with one hand. The device can optionally contain integral testing or analysis component (83) for receiving the sample and providing testing or analysis indication or readout for the user. A method involves piercing the skin at a rapid rate, kneading the surrounding area by ultrasonic action, piezoelectric or mechanical oscillation to stimulate the blood flow from the wound, drawing the fluid using a pumping system.</p>																								

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		

## BLOOD AND INTERSTITIAL FLUID SAMPLING DEVICE

### Field of the Invention

The present invention relates to devices and methods for obtaining samples of blood and other fluids from the body for analysis or processing.

### 5 Background of the Invention

Many medical procedures in use today require a relatively small sample of blood, in the range of 5 - 50 µL. It is more cost effective and less traumatic to the patient to obtain such a sample by lancing or piercing the skin at a selected location, such as the finger, to enable the collection of 1 or 2 drops of 10 blood, than by using a phlebotomist to draw a tube of venous blood. With the advent of home use tests such as self monitoring of blood glucose, there is a requirement for a simple procedure which can be performed in any setting by a person needing to test.

Lancets in conventional use generally have a rigid body and a sterile 15 needle which protrudes from one end. The lancet may be used to pierce the skin, thereby enabling the collection of a blood sample from the opening created. The blood is transferred to a test device or collection device. Blood is most commonly taken from the fingertips, where the supply is generally excellent. However, the nerve density in this region causes significant pain in 20 many patients. Sampling of alternate site, such as earlobes and limbs, is sometimes practiced to access sites which are less sensitive. These sites are also less likely to provide excellent blood samples and make blood transfer directly to test devices difficult.

Repeated lancing in limited surface areas (such as fingertips) results in 25 callous formation. This leads to increased difficulty in drawing blood and increased pain.

To reduce the anxiety of piercing the skin and the associated pain, many spring loaded devices have been developed. The following two patents are representative of the devices which were developed in the 1980s for use with 30 home diagnostic test products.

U.S. Patent No. 4,503,856, Cornell et al., describes a spring loaded lancet injector. The reusable device interfaces with a disposable lancet. The lancet holder may be latched in a retracted position. When the user contacts a release, a spring causes the lancet to pierce the skin at high speed and then retract. The  
5 speed is important to reduce the pain associated with the puncture.

U.S. Patent No. 4,517,978, Levin et al., describes a blood sampling instrument. This device, which is also spring loaded, uses a standard disposable lancet. The design enables easy and accurate positioning against a fingertip so the impact site can be readily determined. After the lancet pierces the skin, a  
10 bounce back spring retracts the lancet to a safe position within the device.

In institutional settings, it is often desirable to collect the sample from the patient and then introduce the sample to a test device in a controlled fashion. Some blood glucose monitoring systems, for example, require that the blood sample be applied to a test device which is in contact with a test instrument. In  
15 such situations, bringing the finger of a patient directly to the test device poses some risk of contamination from blood of a previous patient. With such systems, particularly in hospital settings, it is common to lance a patient, collect a sample in a micropipette via capillary action and then deliver the sample from the pipette to the test device.

20 U.S. Patent No. 4,920,977, Haynes, describes a blood collection assembly with lancet and microcollection tube. This device incorporates a lancet and collection container in a single device. The lancing and collecting are two separate activities, but the device is a convenient single disposable unit for situations when sample collection prior to use is desirable. Similar devices are  
25 disclosed in Sarrine, U.S. Pat. No. 4,360,016, and O'Brien, U.S. Pat. No. 4,9249,879.

30 U.S. Patent Nos. 4,850,973 and 4,858,607, Jordan et al., disclose a combination device which may be alternatively used as a syringe-type injection device and a lancing device with disposable solid needle lancet, depending on configuration.

U.S. Patent No. 5,318,584, Lange et al., describes a blood lancet device for withdrawing blood for diagnostic purposes. This invention uses a rotary/sliding transmission system to reduce the pain of lancing. The puncture depth is easily and precisely adjustable by the user.

5        Suzuki et al., U.S. Patent No. 5,368,047, Dombrowski, U.S. Patent No. 4,654,513 and Ishibashi et al., U.S. Patent No. 5,320,607, all describe suction-type blood samplers. These devices develop suction between the lancing site and the end of the device when the lancet holding mechanism withdraws after piercing the skin. A flexible gasket around the end of the device helps seal the  
10      end around the puncture site until adequate sample is drawn from the puncture site or the user pulls back on the device.

U.S. Pat. No. 4,637,403, Garcia et al. and U.S. Pat. No. 5,217,480, Haber et al, disclose combination lancing and blood collection devices which use a diaphragm to create a vacuum over the wound site.

15      International Application Publication Number WO 95/10223, Erickson et al, describes a means of collecting and measuring body fluids. This system uses a disposable lancing and suction device with a spacer member which compresses the skin around the lance/needle.

Single use devices have also been developed for single use tests. i.e.  
20      home cholesterol testing, and for institutional use to eliminate cross-patient contamination multi-patient use. Crossman et al, U.S. Pat. No. 4,869,249, and Swierczek, U.S. Pat. No. 5,402,798, also disclose disposable, single use lancing devices.

Even with the many improvements which have been made, the pain  
25      associated with lancing remains a significant issue for many patients. The need for blood sampling and the fear of the associated pain is also a major obstacle for the millions of diagnosed diabetics, who do not adequately monitor their blood glucose due to the pain involved. Moreover, lancing to obtain a blood sample for other diagnostic applications is becoming more commonplace, and a  
30      less painful, minimally invasive device is needed to enhance those applications and make those technologies more acceptable.

An object of the present invention is to provide a device and a method for obtaining a sample of bodily fluid through the skin which is virtually pain free and minimally invasive.

Another object of this invention is to provide a method which can result  
5 in a sample of either blood or interstitial fluid, depending on the sample site and the penetration depth utilized. While there are no commercially available devices utilizing interstitial fluid (ISF) at this time, there are active efforts to establish the correlation of analytes, such as glucose, in ISF compared to whole blood. If ISF could be readily obtained and correlation is established, ISF may  
10 be preferable as a sample since there is no interference of red blood cells or hematocrit adjustment required.

Another object of this invention is to provide a method which can draw a small but adjustable sample, i.e. 3 µL for one test device and 8 µL for another test device, as appropriate.

15 Another object of this invention is to provide a method by which the drawn sample is collected and may be easily presented to a testing device, regardless of the location of the sample site on the body. This approach helps with infection control in that multiple patients are not brought in contact with a single test instrument; only the sampling device with a disposable patient-  
20 contact portion is brought to the test instrument. Alternatively, the disposable portion of a test device may be physically coupled with the sampler so the sample can be brought directly into the test device during sampling. The test device may then be read in a test instrument if appropriate or the testing system can be integrated into the sampler and the test device can provide direct results  
25 displayed for the patient.

It is a further object of the invention is to provide a device for minimally invasive sampling comprising a reusable sampler and disposable sample collection.

#### Summary of the Invention

30 In one aspect, the present invention relates to a device which uses mechanical motion to pierce the skin, and a mechanical kneading or oscillation

to produce a sample of fluid from the body and may employ a back pressure or vacuum to collect a small fluid sample into the device. More specifically, the present invention comprises a reusable sampling device and a disposable piercing/collecting apparatus. The device may also employ a back pressure, 5 capillary or vacuum to collect a small fluid sample into the piercing/collecting apparatus that may later be discharged to deliver the collected sample to a test device or other appropriate vessel. The system may alternately be used to deliver the sample to an integral disposable test device, without collecting and separately dispensing the body fluid sample.

10 A method aspect of this invention involves piercing of the skin at a rapid rate (to minimize pain), with a needle (which minimizes the trauma and pressure-associated pain response which occurs with a traditional lancet). The skin is kept taut during the lancing to allow accurate and repeatable penetration of the needle into the skin. After piercing the skin, the needle is withdrawn

15 from the wound and the surrounding area kneaded by ultrasonic action, piezoelectric or mechanical oscillation or squeegee motion to stimulate the blood flow into and from the wound. Additionally heat, electrical potential or friction can be used to stimulate additional flow of the body fluid. This fluid or blood flow can also be stimulated by ultrasonic vibration of the skin surrounding the 20 wound. In an alternate embodiment to stimulate blood flow, the needle remains in the wound for a period of time, with either slow mechanical vibration or rotation of the needle, ultrasonic, or piezoelectric oscillation of the needle, to keep the wound open for blood to pool. After the area has been stimulated and the blood wells up in the wound, a capillary, syringe or pumping system is used 25 to draw microliter samples from the patient. Suction is applied to the needle or the suction tube through either peristalsis, convection (application of heat to a capillary tube) or by the piston of a small microsyringe. The piston is pulled back into the sampler device with spring action, generating a vacuum in the barrel of the microsyringe and quickly drawing fluid from the body through the 30 needle or the suction tube into the barrel to normalize the pressure differential. The piston or suction device then can be reversed to dispense the collected

- sample. The system can also use a capillary tube which is used to draw the sample after it has been collected on the skin surface. The capillary tube can then dispense the sample to a desired test or analysis device by applying pressure through the tube or simply contacting the end of the tube and the
- 5      sample with a surface or material that has sufficient affinity for the fluid to pull the sample from the tube.

The above method and system may be used on various parts of the body. It is particularly appropriate for use on sites other than the fingertips. Although fingertips provide good blood flow, the high density of pain receptors provide

10     for easy access to blood but maximum pain in sampling. The method of this invention actively draws a sample from the body, enabling the use of sampling sites on the body which are inadequate for traditional lancing. Since the method can also provide a mechanism for the easy transfer of the sample, the difficulty of bringing the sample to a test device is eliminated. An important benefit of

15     this system is that the use of alternate sites on the body reduces the accompanying pain sensation and encourages more frequent use as needed.

While the method may be readily used to obtain a blood sample in a minimally invasive fashion, a sample of interstitial fluid may similarly be obtained, generally utilizing a less deep puncture in sites with lower blood flow.

20     This will become more important as tests are developed which can utilize ISF samples, which may be preferred compared to blood.

This invention provides a device and method for lancing a patient and virtually simultaneously producing and collecting the fluid sample, which may be transferred to a test device. A preferred device of the present invention

25     comprises a blood collection system including a lancing needle, drive mechanism, kneading or vibration mechanism and optional suction system and sample ejection mechanism. The device is preferably sized to be hand-held in one hand and operable with one hand. The device can optionally contain integral testing or analysis component for receiving the sample and providing

30     testing or analysis indication or readout for the user.

The lancing needle and firing mechanism designed to create a wound which will both provide an adequate sample but which will still close and heal quickly. Wound healing is an especially important consideration for diabetic patients who often have compromised circulatory systems and slow healing processes. The wound must have a geometry which allows for a momentary space in which blood can fill, taking into account the elastic nature of the skin tissues. Careful consideration must be given to these geometries or the dermis will seal around the lancing needle tip, precluding the drawing of a sample through the tip. In a preferred embodiment a needle is used in combination with a flexible collar and outer tube to spread the wound so blood can pool. Alternatively a multiple needle lancing device can be used to generate a wound which disrupts multiple capillary areas to quickly provide large sample size, but the smaller multiple wounds, can heal more easily.

In an alternate embodiment, the needle/lance is withdrawn from the wound, and the area surrounding the wound is massaged or stimulated to prevent it from closing and to promote the flow of body fluids and or blood to the wound and to the surface of the skin.

Devices according to this invention create a lancing motion which cuts into the small but plentiful capillaries in the superficial vascular plexus under the epidermis. This vascularized region starts at a depth of 0.3 - 0.6 mm from the surface of the skin in many accessible areas throughout the body (forearm, thigh, abdomen, palm). Blood is in plentiful supply in this region of the skin, and healing of small wounds is not problematic. However, bringing a sizable drop of blood to the surface is more problematic than with a finger stick. A finger stick is typically massaged to increase momentary blood flow. This invention provides a system for mechanically massaging a lance site at other body locations by several different approaches, including oscillating an annular ring surrounding the wound to pump the blood surrounding the wound into the wound for extraction by a needle or capillary tube or oscillating paddles or other members adjacent the wound to achieve the desired blood flow. Further, bringing a drop of blood from the skin in other regions of the body, e.g., the

thigh, to a small area on a test device is very difficult. An alternate embodiment of the present invention works with the needle remaining in the wound and the needle being mechanically manipulated to promote the formation of a sample of body fluid in the wound.

5       The needle may be vibrated in any desired and effective motion, including an up and down motion, a side to side motion, a circular motion, a rotation motion or any combination thereof. This creates a momentary opening in which the blood can fill while the device draws the blood through the needle into the disposable sample collection chamber. The vibration of the needle may  
10      occur across a broad range, from 30 cycles per minute up to 1000 cycles per minute or more. This slight vibration does not measurably increase the sensation felt by the patient, particularly when a short duration time is used, but does markedly increase the sample volume which may be easily withdrawn from a given wound and the rate at which the sample volume is produced from the  
15      wound. The oscillation can cause the needle to move up to 2 - 3 mm per cycle. The optimal needle oscillation is less than 1.5 mm, with about 0.5 mm preferred based on current investigations. Oscillating or rotating the needle from 30 cycles per minute up to 1000 cycles per minute or more holds the wound open and prevents it from closing and stopping sample collection and provides sample  
20      collection in a shorter amount of time.

Lancing conventionally occurs at a 90 degree angle (perpendicular) to the skin surface. However, we have found that the lancing member may puncture significantly more capillaries if the lancing is performed on an angle. At a too shallow angle, no significant depth of penetration is achieved. Lancing at an  
25      incident angle of 15 - 90 degrees to the surface of the skin is effective, with shallower angles producing greater blood flow.

The device and system of this invention can further enhance blood flow by massaging the site prior to lancing, as well as by massaging the area adjacent the lancing cite while the lancing member is in the wound and after it is  
30      removed from the wound, as well as during sample collection, as described

above. Alternate methods can use a wiper to rub across or vibrate the skin or can apply heat to the skin to increase the blood flow to the sampling site.

- In another alternate configuration, the lancing needle may be withdrawn very slightly from the point of maximum penetration to create an opening in which blood can pool before being suctioned through the device. This can be accomplished with a double stop system which stops the needle at maximum penetration then stops the retraction of the needle at partial but not full retraction. The area surrounding the wound can be kneaded or massaged by optional movable members mechanical to stimulate blood flow to the wound and increase the sample size and the rate of production of the sample. The mechanical motion can displace the area around the wound from 0.05 to 8 mm, with 1 - 5 mm being preferred based on current investigations. A wiper device can be used in the aspect which rubs the skin to increase the blood flow to the wound by stimulating the capillaries.
- The mechanical stimulation of the wound can be accomplished by different methods or motions and members. An annular ring or other polygon or blade or paddle members may be oscillated around the wound by piezoelectric, ultrasonic, solenoid/coil, motor and cam or other methods apparent to one skilled in the art. Mechanical oscillation in the range of 2 to 1000 cycles per minute may be employed, with 10 to 400 cycles being preferred. Ultrasonic vibration has been effective at a frequency as high as 40 kHz. Alternately, the device may employ a blade or squeegee type of stimulator which kneads the site with horizontal or a combination of horizontal and vertical action and promotes blood flow to the wound. The squeegee may act on the wound area 2 to 200 times per minute, with 60 times per minute preferred based on current investigations. Additionally, the needle may be vibrated ultrasonically, with or without the kneading or massaging action adjacent the wound. The ultrasonic vibration can cover the range of ultrasonic frequencies depending on the sampling area and whether the needle or the stimulation device is being activated.

In another aspect of this invention the lancing member is contained a multi-chambered or multi-channelled capillary disposable member wherein one chamber contains the lancing member and an adjacent chamber is adapted to receive the blood or fluid exiting the wound. The multi-chambered capillary

5      disposable can be made from any suitable material, and installed in the sampler so that it is positioned in the appropriate position relative to the wound created to permit collection of the sample. The lancing device is driven into the skin and withdrawn by the secondary retraction springs after reaching the limit stops. After withdrawal of the lancing member, the stimulator ring or other polygon

10     shape is oscillated by one of the various methods to pump blood from the capillaries adjacent to the wound. The sampling device of this aspect of the invention has stop mechanisms to limit the penetration of the lancing member and sample duration system which sets the time of the sample collection. The lancing guide chamber can be formed a variety of ways and one skilled in the

15     art can reconfigure it to create alternate embodiments.

In another aspect similar to the above, the lancing member can be contained within a single capillary tube and adapted to extend from the end of the tube to create the wound. The lancing member then retracts a sufficient distance inside the capillary to allow the desired sample to be collection in the

20     end of the same capillary tube in the space below the retracted lancing member. In such an embodiment the lancing member can be vibrated in the wound before retraction, also as described above.

To achieve the sample collection after withdrawing the needle, a stimulator ring can be used to pump the sample from the surrounding capillaries

25     through the wound opening. The stimulator ring is designed to keep the skin taut to allow better penetration of the skin during lancing and help keep the wound open during pumping. It can be oscillated appropriately to insure that enough sample is pumped from the local capillaries. The time or number of cycles varies by individual and location being sampled. To achieve a variable

30     sample time either of the following methods may be used. A sensor can be built into the sampler which senses the blood in the collection chamber or

device. When an adequate sample level (which may be adjustable) is reached, the stimulation mechanism is turned off. A second method is to have a patient definable input which sets the time duration for the test or the number of cycles for the stimulation ring. Additional stimulator motions can be employed to

5 promote the extraction of bodily fluids. These include sinusoidal motion, wobbling, kneading or peristaltic motion. An alternate stimulator device can be designed with an inner and outer ring which will alternate creating a peristaltic pumping motion on the capillaries surrounding the wound. Another alternate stimulator device uses a spiral spring that can be compressed flat to emulate

10 multiple pumping rings. As will be apparent, various configurations of multiple stimulator rings, paddles, or other members, used in various rhythms and orders of movement can be employed in the present invention. The stimulator ring or member can be heated in order to heat the skin to increase the capillary volume flow to and out of the wound. In addition, the housing or case of the device or

15 other components of the device can be heated to provide heating of the skin.

In another aspect of the invention a diffused laser may be used to penetrate to the superficial vascular plexus and a capillary tube may be used to collect the sample. A lens may be used to diffuse the laser so that it does not create a large wound or damage large areas of skin and tissue. A minimum

20 wound size is important to enable rapid healing. The capillary collection tube can use a suction generator to draw the sample up the tube and can also utilize an optional stimulator ring to pump the blood from the adjacent capillary beds.

In another aspect of the invention the lancing can be accomplished by a pulse of a fluid under high pressure such as a liquid or a compressed gas. In

25 addition the compressed gas can be directed, at lower pressure, to the skin surface to massage the skin before lancing, during lancing and/or during sample collection. Pulsing the compressed gas against the skin at desired pressures, patterns and intervals, including sequential pattern across the surface of the skin, can provide the desired stimulation of the blood flow into and from the wound.

30 The pulse of compressed gas used to perform the lancing and opening of the wound can be a single pulse or multiple pulses, can be directed through a

capillary sample collection tube, and/or can be applied vertically to the skin surface or at an angle, as described above for other lancing members, to achieve puncturing the maximum capillaries in the skin and provide the sample collection in a short period of time.

5        In another aspect of the invention an off meter test device is used with a sampler of this invention to provide an integrated sampling and testing device. This device can be used by the patient to essentially simultaneously draw a sample and test for the presence or concentration of an analyte in a body fluid. The sample can be taken from an alternate location other than the fingertips  
10      with the device of this invention. To accomplish this it is critical to the test to provide a mechanism to stimulate the wound and or the surrounding area to provide an adequate sample for the test device. This stimulation can be accomplished by manipulating the needle or the area of skin surrounding the wound as described above. A combination of the two methods can be employed  
15      to increase the volume and/or decrease the sampling time. The sample is introduced directly into a test device or testing area rather than being collected and subsequently dispensed.

In another aspect, this invention also provides a method of determining the correct sample size prior to transferring or testing. Different methods can be  
20      used to sense the volume and/or presence of the sample. One system uses two contacts to sense the presence and/or volume of a sample. The body fluid either is drawn up a tube or wells up on the surface of the skin where it creates a short between two contacts which signal that the proper sample has been drawn. An alternate system uses an LED and receiver. When the sample rises to the level  
25      where it blocks the LED from the receiver the proper sample has been drawn. Other optically activated or contact activated systems can be used in this aspect of the invention.

In another aspect, this invention also provides a method of making a unit with a disposable section to limit biohazard cross contamination.  
30        In another aspect, this invention provides a bell shape capillary tube. The capillary tube wicks the sample up the tube until it reaches the transition of

the bulb. The bulb is then depressed to expel the sample or a known volume of the sample to a desired location, such as a test strip or device for analysis. The bell shape can be designed as a cone and the sample is wicked up the cone and dispensed by reversing the cone and expelling the sample by capillary action  
5 onto the test device.

In an alternate embodiment the device of this invention lances and stimulates the area, creating a drop of sample fluid, which is collected on or transferred directly to a test device by applying the test device to the drop.

In another aspect, this invention can also include an auto-injection  
10 device. A preloaded tip may be placed into the barrel. The trigger and spring system can be designed to deliver the sample from the syringe rather than to collect a sample into the syringe. One who is skilled in the art could readily reconfigure the mechanism described to inject a sample. Moreover, the device may have dual function of collecting a sample while simultaneously or  
15 sequentially injecting a sample, which can be in response to a test performed in the device on the sample collected.

#### Brief Description of Drawings

Figure 1 shows a device of this invention having a double stop mechanism.

20 Figure 2A and Figure 2B are cross section views of a device of this invention in the cocked and the deployed position, respectively.

Figure 3 shows a longitudinal cross section of a device according to this invention having a stimulator member proximate to the lancet or needle.

25 Figure 4 shows the stimulator member positioned on the skin of the patient adjacent the wound and the lance.

Figure 4A provides a schematic layout of the skin illustrating where the superficial vascular plexus capillaries are relative to the skin's surface.

Figure 4B is a representation of a wound, shown in cross section, which will facilitate the formation of a small pool of blood yet ensure that the skin  
30 will fully contract around the wound following sampling to promote healing.  
The relationship of the wound, needle and the superficial vascular plexus

capillaries is also illustrated. In the embodiment shown the capillary is offset in the needle.

Figures 4C and 4D show alternative embodiments in which, to enhance sample collection and minimize the wound size required, the needle may be  
5 vibrated mechanically in either an up and down motion as shown in Figure 4C or a side to side as shown in Figure 4D.

Figure 4E shows that the needle may be vibrated ultrasonically with or without the kneading or massaging action.

Figures 4F and 4G show that the area surrounding the wound can be  
10 kneaded by optional mechanical motion to stimulate blood flow to the wound and increase the sample size and the rate of production of the sample.

Figure 4H shows that, alternately, the device may employ a squeegee type of stimulator which kneads the site with horizontal or a combination of horizontal and vertical action and promotes blood flow to the wound.

15 Figure 4I shows an alternate embodiment in which needle is oscillated or rotated.

Figures 5A and 5B show front and side views of a replaceable needle with a spade tip design adapted for use in this invention, especially for a moving/rotating needle for holding a wound open during sample collection.

20 Figures 6A and 6B illustrate a front and side view of a disposable needle that has an eccentric passageway for sample collection. The needle can have a luer lock type connection to the sample device of this invention.

Figure 7 shows a needle with a collar or sleeve to provide mechanical spreading of the wound during sample collection.

25 Figures 8A and 8B are longitudinal cross section views of a device with a multi-chambered capillary members accommodating a lancet or needle in one chamber and providing another chamber or conduit for sample collection.

Figures 8C, 8D and 8E are top view cross section views of two and three chamber capillary members.

Figure 9A and 9B illustrate a longitudinal cross section of a device having a multi-chambered capillary disposable and peristaltic pump to collect a sample.

5 Figure 9C illustrates in cross section an alternate suction/standoff/lance disposable tip containing contacts for electrically sensing the presence and/or volume of body fluid.

Figure 10 illustrates in cross section a device with a laser positioned to radiate through the interior of the needle or capillary for piercing the skin.

10 Figure 11 illustrates in longitudinal cross section in cross section a device of this invention for use with a combined suction/standoff chamber as part of a disposable sample collection system.

Figures 12A and 12B illustrate a longitudinal cross section and side view cross section of a device of this invention having an angled lancet or needle and employing an absorbent strip.

15 Figures 13 and 14 show a longitudinal cross section and a side view cross section of a sampling device of the present invention with an integrated colorimetric instrument test.

Figure 15 shows a longitudinal cross section of a sampling device of the present invention with an integrated electrochemical test.

20 Figures 16 and 17 show a longitudinal cross section and a side view cross section of a sampling device of the present invention with an integrated colorimetric visual test.

Figure 18 shows an alternate device which has a completely disposable lower section to minimize blood contamination between uses.

25 Figure 19A shows the combination of a dual alternating stimulation ring system.

Figure 19B shows the device with a telescoping stimulator ring.

Figures 20A, 20B and 20C illustrate a bell shape capillary tube and Figure 20D shows a straight capillary tube with a test strip.

30 Figure 21 illustrates a device of this invention with a member to oscillate the needle to stimulate fluid flow from the wound.

Figure 22A shows a multiple needle lancing device.

Figure 22B shows a broader single lancet.

Figures 22C and 22D show a die cut sheet which has small multiple barbs formed in the sheet for use as a lance in the present invention.

5    Description of the Invention

Figure 1 illustrates a minimally invasive sampling device according to the invention. The device is comprised of numerous components which will be more fully described below. The main body 1 supports the various mechanical components housed within the device.

10      The main body 1 comprises an elongated hollow cylindrical tube with openings at both ends. The sampling needle 16 which is part of the disposable 3 which is capable of being retracted or deployed so that it can protrude beyond the needle guard 17 is positioned at one end. The arming and dispensing plunger 22 protrudes from the other end. The device has a needle guard 17  
15      which permits the loading of the disposable 3. Disposable 3 is attached to the syringe 13 and plunger 14 is released by the suction cam 8.

20      The syringe 13 is captivated to the drive system by syringe clamp 12 which has the main tie rods 4 anchored to it. The main drive springs 11 are captivated between the syringe clamp 12 and cross support 10 and the tie rods 4 are threaded through them.

25      The main tie rods 4 have the main cams 9 attached to them and are supported by the activation trigger 2 prior to release. The secondary springs 21 and secondary stops 20 provide a mechanism after activation to pull the needle back out of the wound to permit blood accumulation. When the skin is pierced the secondary springs 20 retract the needle from the wound triggering the suction cam 8 and plunger 14 is released. The arming and dispensing plunger 22 is a dual purpose device. When the patient pulls up, it preloads the drive springs 11. It is latched by pushing in on the activation trigger 2.

30      The stop and adjustment tabs 19 control the depth of penetration of the needle 16 so that the optimal depth of penetration is reached for a particular sample site. The sample 15 is drawn from the patient when the device has been

deployed by releasing the activation trigger 2 and the needle 16 has been retracted from the patient.

The system shown in Figure 2A and 2B is comprised of a reusable barrel 1 and associated mechanisms and a sterile disposable 13. The disposable 13 has 5 an ultra fine gauge needle 16 which is imbedded in a cap until the device is readied for use. Figure 2B shows the device in the deployed state with a sample in disposable 13 and figure 2A shows it undeployed.

Main yoke 3 is held by activation triggers 2 which support the main tie rods 4 when the system is undeployed. The system is activated by releasing the 10 activation triggers 2. This releases the main cam 9 which causes the syringe to be deployed by the drive spring 11 which is captured between the cross support 10 and the syringe clamps 12. The needle 16 pierces the skin as a result of these actions and the penetration depth is controlled by stop 27. When the suction cams 8 is released by the secondary trigger 5, the suction spring 6 is 15 released. This drives the suction yoke 7 up slowly due to the damping action of the syringe plunger 14 so a back pressure or vacuum is created in the syringe body. Sample 15 is actively drawn into the syringe.

The sample can be delivered easily and precisely to a test device or other container by pressing down on a button on the top of the sampler. The 20 disposable syringe 13 and needle 16 may be imbedded in the cap in which it was shipped or placed into a Sharps container for safe disposal.

To insure that adequate sample size is collected the needle 16 can be vibrated, oscillated or rotated to keep the wound from closing. The disclosure of Figures 3, 4, 4C, 4D, 4E, 4I, 9, 12 and 13 show and describe various 25 alternative motions that can be used to accomplish this.

Another version of this device is also capable of performing as an auto-injection device. A preloaded tip may be placed into the barrel. The trigger and spring system can be designed to deliver the sample from the syringe rather than to collect a sample. One who is skilled in the art could readily reconfigure 30 the mechanism described to inject a sample.

Figure 3 illustrates a minimally invasive sampling device according to the invention. The device is comprised of numerous components which will be more fully described below. The main body 1 supports the various mechanical components housed within the device.

5       The main body 1 comprises an elongated hollow cylindrical tube with openings at both ends. The sampling needle 16 which is part of the disposable 3 which is capable of being retracted or deployed so that it can protrude beyond the needle guard 17 is positioned at one end. The arming and dispensing plunger 22 protrudes from the other end. The device has a needle guard 17  
10      which can be slid up and down main body 1 by the patient to permit the loading of the disposable 3. Disposable 3 is attached to the syringe 13 by the tip adapter 18. The internal parts of the syringe 13 are the plunger 14 which is activated by the suction spring 6 and the suction yoke 7. The plunger is released when the suction cam 8 is released by the secondary trigger 5.

15      The syringe 13 is captivated to the drive system by syringe clamp 12 which has the main tie rods 4 anchored to it. The main drive springs 11 are captivated between the syringe clamp 12 and cross support 10 and the tie rods 4 are threaded through them.

20      The main tie rods 4 have the main cams 9 attached to them and are supported by the activation trigger 2A prior to release. The secondary springs 21 and secondary stops 20 provide a mechanism after activation to pull the needle back out of the wound to permit blood accumulation. When the skin is pierced the secondary springs retract the needle from the wound and initiate the stimulation ring 25 oscillation system 26 and 27 to force blood flow to the  
25      wound. The arming and dispensing plunger 22 is a dual purpose device. When the patient pulls up, it preloads the drive springs 11. It is latched by pushing in on the activation trigger 2A.

30      The stop and adjustment tabs 19 control the depth of penetration of the needle 16 so that the optimal depth of penetration is reached for a particular sample site. The stimulator ring can be deployed during lancing to keep the skin taut, thus allowing more accurate and repeatable penetration of the skin.

The sample 15 is drawn from the patient when the device has been deployed by releasing the activation trigger 2 and the needle 16 has been retracted from the patient.

Figure 4 illustrates the relationship of the needle 16, wound 200 and stimulation ring 25. The detail areas of the skin are shown for clarity. The stimulator ring 25 is used to pump the sample of body fluid 61 into wound area 200. A singular stimulation ring 25 is shown in this illustration. However, multiple telescoping rings may be employed to enhance the blood transport.

The stimulation ring can also be formed to with a series of notches to permit the resupply of body fluid to the capillaries when the stimulation ring 25 is retracted from the wound site 200.

In an alternate embodiments the stimulation ring is heated or a secondary motion added to act as a wiper to enhance the flow of body fluid to the wound 200. Other members can be used instead of a ring to provide the stimulation desired.

Figures 4C, 4D and 4E illustrate that the needle may be vibrated in the desired motion. This creates a momentary opening in which the blood can fill while the device draws the blood through the needle into the disposable sample collection chamber. The vibration of the needle may occur across a broad range, from 30 cycles per minute up to 1000 cycles per minute or more. This slight vibration does not measurably increase the sensation felt by the patient but does markedly increase the sample volume which may be easily withdrawn from a given wound and the rate at which the sample volume is produced from the wound. The oscillation can cause the needle to move up to 2 - 3 mm per cycle. The optimal needle oscillation is less than 1.5 mm, with about 0.5 mm preferred based on current investigations. Lancing generally occurs at a 90 degree angle (perpendicular) to the skin surface. However, the lancing member may puncture significantly more capillaries if the lancing is performed on a angle. At a very shallow angle, no significant depth of penetration is achieved.

Lancing at an incident angle of 15 -90 degrees to the surface of the skin is effective, with shallower angles producing greater blood flow. The ultrasonic

vibration can cover the range of ultrasonic frequency depending on the sampling area and whether the needle or the stimulation device is being activated.

Figures 4F and 4G show massaging or kneading the area surrounding the wound. The mechanical motion can displace the area around the wound from 5 0.05 to 8 mm, with 1 - 5 mm being preferred based on current investigations. Figure 4G shows a wiper device which rubs the skin to increase the blood flow to the wound by stimulating the capillaries. This action can also be done by the patient by rubbing the area to increase the blood flow to the sampling site prior to taking a sample. The oscillation can be accomplished via piezoelectric, 10 ultrasonic, or by using a solenoid/coil or a motor and cam. Mechanical oscillation in the range of 2 to 1000 cycles per minute may be employed, with 20 to 200 cycles being preferred. Ultrasonic vibration has been effective at a frequency as high as 40 kHz. Figure 4F shows an alternate embodiment in which the wound is mechanically stimulated such as by an annular ring which 15 may be oscillated.

Figure 4H shows massaging with a squeegee type of stimulator. Such a squeegee may act on the wound area 2 to 200 times per minute, with 60 times per minute being preferred.

Figure 4I shows rotating or oscillating the needle from 30 cycles per 20 minute up to 1000 cycles per minute or more. This holds the wound open and prevents it from closing and stopping sample collection. This embodiment can employ the needles disclosed herein in Figures 4B, 5A, 5B, 6A and 6B, conventional needles or round or flat lancets.

Figures 5A and 5B show a spade tip needle/lance profile which is used 25 by the invention to create a void area in the wound. Figures 5A and 5B show one needle profile which is useful in implementing this embodiment. The spade end helps create a void area when it is rotated in the small wound.

Figures 6A and 6B show an asymmetric needle design to create a wound 30 which can enhance capillary blood collection. Needle 16 is molded to form disposable 3. Another aspect of the invention is the provision of an easily replaceable lancing tip (Figure 6A and 6B). The tip must attach to the device

simply to facilitate the availability of a fresh, sterile needle for each sample drawn. A wide range of lancet or needle gauges may be used for the tip. Current investigations show that 10 through 32 gauge is acceptable depending on the sampling location. The entire device may also be designed as a single  
5 use device. In this configuration, the device would be precocked and would only trigger and dispense once. A new device with a sterile tip would be thus used for each sample drawn. It will be apparent that an alternate disposable can be constructed from a needle and flexible tube. The tube acts as a reservoir for the sample as it is drawn by the applied vacuum. Another capillary type  
10 disposable is shown in figure 31. The bell type disposable uses capillary action to wick the sample up the tube until it reaches the bulb or vacuum created by depressing the bulb. The sample is dispensed by collapsing the bulb. Anyone skilled in the art would be able to readily reconfigure the design presented herein to be a single use device.  
15 Figure 7 illustrates the use of a needle 16 with a flexible collar 225 and stimulator ring 25 to hold the wound open during the extraction of the body fluid sample. The collar 225 is affixed to the needle and acts as a stop and as a means of spreading the wound. This provides a means of forcing the wound open during sampling. The collar 225 can be fashioned in various  
20 configurations to achieve the same results by one skilled in the art.

Figure 8A shows the lancing member is part of a multi-chambered capillary disposable. Figure 8B provides an exploded view of the end of the device showing the relation ship of lancet 30, disposable 33 and lancet guide tube 35. The multi-chambered capillary disposable can be made from any  
25 suitable material. Figures 8C, 8D and 8E show various alternatives of this embodiment. One skilled in the art could readily reconfigure a disposable which would be equal to this invention.

The lancet 30 creates the wound and is guided by guide tube 35. The sample is drawn up the sample collection tube/disposable 33. The complete  
30 device can either be fashioned as one single disposable or multiple components.

Figures 9A illustrates a minimally invasive sampling device according to the invention using the alternate capillary disposable blood collection device Figure 8A which is disposable 33. The device is comprised of numerous components which will be more fully described below. The main body 1 5 supports the various mechanical components housed within the device. Figure 9B shows the cutout to allow communication of blood to the sample collection tube.

The main body 1 comprises of an elongated hollow cylindrical tube with openings at both ends. The capillary sampling disposable with lancing member 10 30, which is part of disposable 33 and is capable of being retracted or deployed so that it can protrude beyond the end of the main body 1, is positioned at one end. The arming plunger assembly 36 protrudes from the other end. The lancing member 30 is guarded by being withdrawn into the needle guide tube 35 which is part of the disposable 33. The needle guide tube 35 acts as the lancing 15 guide and lancet guard. The disposable 33 is attached to the main body 1 so that it is positioned at the appropriate location to guide the lancet and suction up the blood. The striker 39 is projected so as to drive the lancet into the patient 41 by the spring 43 and the arming plunger assembly 36. The arming plunger is locked in place by a cam 45 and trigger 47. A double stop return spring 49 20 is located and sized to return the lancet 30 back into the disposable 33 needle guide tube 35. The needle guard 17 supports the main body 1 on patient 41.

The double stop return springs 49 provide a mechanism after activation to pull the needle back out of the wound to permit blood 61 accumulation. When the skin is pierced the secondary springs 49 retract the needle from the 25 wound and initiate the stimulation ring 25 oscillation system to force blood flow to the wound. The stimulator ring can oscillate in the preferred range of 1 to 5 mm. The frequency can vary from 5 to 1000 cycles per minute in the preferred embodiment. The oscillation of the stimulator ring 25 is driven by the coils 51 which oscillate the stimulator ring 25 to pump the blood 61 from the 30 surrounding capillaries in the skin into the wound. Each down stroke of the stimulator ring 25 provides this pumping action. This pumping action can be

modified to include sinusoidal motion, wobbling, kneading or peristaltic motion which will enhance the blood flow to the wound.

A linkage 53 drives a peristaltic roller system 55 and rollers 57 against the suction tube 59 causing blood 61 to be drawn up the suction tube 59 creating the sample 15.

The stop and adjustment tabs 19 control the depth of penetration of the lancet 30 so that the optimal depth of penetration is reached for a particular sample site.

In another aspect of this invention, electric potential can be applied across the skin to also stimulate blood flow to the wound. This can be accomplished by having separate electrodes present in the device to contact the skin and deliver the electric current at locations desired. Or, the current can be delivered to the skin through components of the device, appropriately insulated internally of course, such as the stimulator ring 25 and sample tube 59, or any other appropriate combination. In general, low voltage DC or AC current can aid in blood flow. The voltage, amperage and cycles (in the case of AC) can be determined by one skilled in the art, but DC voltage in the range of 1 millivolt to 12 volts will be useful. Likewise, the duration of the applied current or the pulsing thereof can be selected as desired. In a particular example tube 33 in Figure 9A or needle 16 in Figure 3 can be the negative electrode and ring 25 in Figure 9A and Figure 3 or guard 17 can be the positive electrode.

Figure 9C illustrates an alternate suction/stand off chamber blood collection device 72 which comprises of lance 30, suction tube 59, secondary tube which guides the lance 30, suction/standoff chamber 105, and contacts 107 and 109. The suction tube 59 is mounted in suction/standoff chamber 105 so as to permit the suction tube to be located off the wound to promote bleeding while the wound is stimulated. The contacts provide a means of determining if the sample size is adequate. Contacts 109 are made when adequate volume of blood is present in the cap 105 and these are in communication with contacts 107 which are in communication with the electronic package of the sampler.

Once contacts 109 are made by the blood then the circuit is completed signaling the system to stop.

Figure 10 illustrates a minimally invasive sampling device according to the invention using the alternate capillary disposable blood collection device and 5 laser 67 lancing mechanism. The device is comprised of numerous components which will be more fully described below. The main body 1 supports the various mechanical components housed within the device.

The main body 1 is comprised of an elongated hollow cylindrical tube with openings at both ends. The capillary sampling disposable with diffusing 10 lens member 60 which is part of disposable 63 is installed in one end of the main body 1. The firing switch 65 protrudes from the other end. The capillary tube 59 acts as the laser guide and sample collection device. The disposable 33 is attached to the main body 1 so that it is positioned at the appropriate location to direct the laser and to suction up the blood. The laser 67 is diffused by 15 going through the lens and creates the wound in the patient.

When the skin is pierced, the laser shuts down. This initiates the stimulation ring 25 oscillation system to force blood flow to the wound. The oscillation of the stimulator ring 25 is driven by the coils 51 which oscillate the stimulator ring 25 so as to pump the blood 61 from the surrounding capillaries 20 in the skin into the wound. Each down stroke of the stimulator ring 25 provides this pumping action. A linkage 53 drives a peristaltic roller system 55 and rollers 57 against the suction tube 59 causing blood 61 to be drawn up the suction tube 59 creating the sample 15. The oscillation of the stimulator ring can have a range of 0 to 8 mm and preferably 1 to 5 mm. The frequency can 25 also vary from 2 to 100 cycles per minute.

In an alternative embodiment for the device of Figure 10, the lancing means can be a liquid under high pressure or a compressed gas pulse instead of the laser. A pulse of compressed gas, or multiple pulses, can be directed at the skin. In addition, the liquid under pressure or compressed gas pulses can be 30 applied in the annular space between ring 25 and housing 1 to massage and stimulate the skin to increase blood flow to the wound.

It is to be understood that the vacuum employed in the various embodiments of this invention can be used with the capillary tubes, such as 59 in Figure 10, as well as the needles of Figures 4B, 5A and B, and 6A and B.

Figure 11 illustrates a minimally invasive sampling device according to 5 the invention using the alternate suction/stand off chamber blood collection device 72 which is more fully described in illustration 9C. The device is comprised of numerous components which will be more fully described below. The main body is 1 which supports the various mechanical components housed within the device.

10 The main body 1 comprises of an elongated hollow cylindrical tube with openings at both ends. The suction/stand off chamber sampling disposable with lancing member 30 which is part of disposable 72 and is capable of being retracted or deployed so that it can protrude beyond the end of the main body 1 positioned at one end. The arming tabs/trigger 37 protrude from the sides of  
15 main body 1. The disposable 72 is attached to the main body 1 so that it is positioned at the appropriate location to guide the lancet and suction up the blood. The striker 39 is projected so as to drive the lancet into the patient 41 by the spring 43 and the arming plunger assembly 37. The arming plunger is locked in place by a cam 45 and trigger 37. A double stop return spring 49 is  
20 located and sized to return the lancet 30.

In another aspect, the capillary sample collection tubes used in the various embodiments of this invention, such as 33 in Figures 8A and 9A, 59 in Figure 9C and 10 and 150 in Figures 20A-20C, can be selected to have an affinity for the sample fluid greater than the skin so the fluid or blood will wick 25 into the tube by capillary action. However, the capillary tube is also selected to have less affinity for the sample fluid or blood than a test strip or test device surface of receiving port so that the sample fluid or blood will wick out of the capillary tube into or onto the test strip or device. Such materials for the capillary tube can easily be determined and selected by one skilled in the art, 30 but generally capillary tubes of nylon, PTFE, and the like generally fulfill this function. It will be recognized that the selection of such material for the

capillary tube must be made relative to the materials present in and the physical construction the test strip or device, if this aspect of the present invention is to be utilized.

The double stop return springs 49 provide a mechanism after activation 5 to pull the needle back out of the wound to permit blood 61 accumulation. When the skin is pierced, the secondary springs 49 retract the needle from the wound and initiate the stimulation ring 25 oscillation system to force blood flow from the wound. The stimulator ring can oscillate in the preferred range of 1 to 5 mm. The frequency can vary from 5 to 1000 cycles per minute in the 10 preferred embodiment. The oscillation of the stimulator ring 25 is driven by the motor 51 which oscillate the stimulator ring 25 to pump the blood 61 in the surrounding skin capillaries from the wound so the blood can flow to the surface of the skin, bead up, and contact the disposable 72. Each down stroke of the stimulator ring 25 provides this pumping action. The disposable 72 is then 15 lowered onto the blood bead using a secondary motion spring 74 that is released by a secondary motion trigger 75, and suction of the blood initiated. The suction device 85 shown here is a mini syringe which is activated by spring 86 when secondary motion trigger 75 is released causing blood 61 to be drawn up the disposable 72. The stop and adjustment cap 19 controls the depth of 20 penetration of the lancet 30 so that the optimal depth of penetration is reached for a particular sample site.

Figures 12A and 12B illustrate a minimally invasive sampling device according to the invention using a disposable piercing apparatus, a reusable sampling device and a disposable absorbent test strip 83. Figure 12A shows the 25 device in a side view and Figure 12B is a front view. The device is comprised of numerous components which will be more fully described below. The main body is 1 which supports the various mechanical components housed within the device.

The main body 1 comprises of an elongated hollow cylindrical tube with 30 openings at both ends. The lancing member 30 which is part of disposable 33 is capable of being retracted or deployed so that it can protrude beyond the end

of the main body 1 is positioned at one end. The arming tabs 37 protrude from the sides of main body 1. The lancing member 30 is guarded by being withdrawn into the tube 35 which is part of the disposable 33. The tube 35 acts as the lancing guide and lancet guard. The disposable 33 is attached to the 5 main body 1 so that it is positioned at the appropriate location to guide the lancet and is held in place by the disposable clamp 3. The striker 39 is projected so as to drive the lancet into the patient 41 by the spring 43 and the arming plunger assembly 36. The arming plunger is locked in place by a cam 45 and trigger 47. A double stop return spring 49 is located and sized to return 10 the lancet 30 back into the tube 35.

The double stop return springs 49 provide a mechanism after activation to pull the needle back out of the wound to permit blood 61 accumulation. When the skin is pierced the secondary springs 49 retract the needle from the wound and initiate the stimulation ring 25 oscillation system to force blood 15 flow to the wound. The cam 55 oscillates the oscillator ring 57 which transmits the motion to stimulation ring 25. The stimulator ring can oscillate in the preferred range of 1 to 5 mm. The frequency can vary from 5 to 1000 cycles per minute in the preferred embodiment. The oscillation of the stimulator ring 25 is driven by the motor 51. The battery 56 provides energy to run the motor 20 51 which oscillates the stimulator ring 25 to pump the blood 61 from the surrounding capillaries in the skin into the wound. Each down stroke of the stimulator ring 25 compresses the stimulator spring 53 which provides the return motion for the stimulator ring 25. The disposable chemical strip 83 is then lowered onto the blood bead using a secondary motion spring 74 that is released 25 by a secondary motion trigger 75. The blood is absorbed by the disposable chemical strip 83 which fits into a slot in the main body 1 and the stimulator ring 25.

The stop and adjustment tabs 19 control the depth of penetration of the lancet 30 so that the optimal depth of penetration is reached for a particular 30 sample site.

Figures 13 and 14 illustrate an integration of the minimally invasive sampling device with a chemical test measurement, such as glucose, and electronic readout according to the invention using a disposable piercing apparatus 33, a reusable sampling device 1, a disposable absorbent test strip 83, 5 and a method of readout such as colorimetric test which is read electronically and has an electronic readout system. Figure 13 shows the device in a side view and Figure 14 is a front view. The device is comprised of numerous components which will be more fully described below. The main body is 1 which supports the various mechanical and electrical components housed within 10 the device.

The main body 1 comprises of an elongated hollow cylindrical tube with openings at both ends. The lancing member 30 which is part of disposable 33 is capable of being retracted or deployed so that it can protrude beyond the end of the main body 1 is positioned at one end. The arming tabs 37 protrude from 15 the sides of main body 1. The lancing member 30 is guarded by being withdrawn into the tube 35 which is part of the disposable 33. The tube 35 acts as the lancing guide and lancet guard. The disposable 33 is attached to the main body 1 so that it is positioned at the appropriate location to guide the lancet and is held in place by the disposable clamp 3. The striker 39 is 20 projected so as to drive the lancet into the patient 41 by the spring 43 and the arming plunger assembly 36. The arming plunger is locked in place by a cam 45 and trigger 47. A double stop return spring 49 is located and sized to return the lancet 30 back into the tube 35.

The double stop return springs 49 provide a mechanism after activation 25 to pull the needle back out of the wound to permit blood 61 accumulation. When the skin is pierced the secondary springs 49 retract the needle from the wound and initiate the stimulation ring 25 oscillation system to force blood flow to the wound. The cam 55 oscillates the oscillator ring 57 which transmits the motion to stimulation ring 25. The stimulator ring can oscillate in the 30 preferred range of 1 to 5 mm. The frequency can vary from 5 to 1000 cycles per minute in the preferred embodiment. The oscillation of the stimulator ring

25 is driven by the motor 51. The battery 56 provides energy to run the motor 51 which oscillates the stimulator ring 25 to pump the blood 61 from the surrounding capillaries in the skin into the wound. Each down stroke of the stimulator ring 25 compresses the stimulator spring 53 which provides the return motion for the stimulator ring 25. . The disposable chemical strip 83 is then lowered onto the blood bead using a secondary motion spring 74 that is released by a secondary motion trigger 75, and suction of the blood initiated. The blood is absorbed by the disposable chemical strip 83 which has been manufactured into the disposable 33. The strip is then read in place by a LED 88  
5 colorimetric system and analyzed by electronics which are part of the device and displayed on display 84.  
10

The stop and adjustment tabs 19 control the depth of penetration of the lancet 30 so that the optimal depth of penetration is reached for a particular sample site.

15 Figure 15 illustrates an integration of the minimally invasive sampling device with a chemical test measurement, such as glucose, and electronic readout according to the invention using a disposable piercing apparatus 33, a reusable sampling device 1, a disposable absorbent test strip 83, and a method of readout such as a electrochemical test which is read electronically and has an  
20 electronic readout system. The device is comprised of numerous components which will be more fully described below. The main body is 1 which supports the various mechanical and electrical components housed within the device.

25 The main body 1 comprises of an elongated hollow cylindrical tube with openings at both ends. The lancing member 30 which is part of disposable 33 is capable of being retracted or deployed so that it can protrude beyond the end of the main body 1 is positioned at one end. The arming tabs 37 protrude from the sides of main body 1. The lancing member 30 is guarded by being withdrawn into the tube 35 which is part of the disposable 33. The tube 35 acts as the lancing guide and lancet guard. The disposable 33 is attached to the  
30 main body 1 so that it is positioned at the appropriate location to guide the lancet and is held in place by the disposable clamp 3. The striker 39 is

projected so as to drive the lancet into the patient 41 by the spring 43 and the arming plunger assembly 36. The arming plunger is locked in place by a cam 45 and trigger 47. A double stop return spring 49 is located and sized to return the lancet 30 back into the tube 35.

- 5       The double stop return springs 49 provide a mechanism after activation to pull the needle back out of the wound to permit blood 61 accumulation. When the skin is pierced the secondary springs 49 retract the needle from the wound and initiate the stimulation ring 25 oscillation system to force blood flow to the wound. The cam 55 oscillates the oscillator ring 57 which transmits  
10      the motion to stimulation ring 25. The stimulator ring can oscillate in the preferred range of 1 to 5 mm. The frequency can vary from 5 to 1000 cycles per minute in the preferred embodiment. The oscillation of the stimulator ring 25 is driven by the motor 51. The battery 56 provides energy to run the motor 51 which oscillates the stimulator ring 25 to pump the blood 61 from the  
15      surrounding capillaries in the skin into the wound. Each down stroke of the stimulator ring 25 compresses the stimulator spring 53 which provides the return motion for the stimulator ring 25. The disposable test strip 83 is then lowered onto the blood bead using a secondary motion spring 74 that is released by a secondary motion trigger 75. and suction of the blood initiated. The blood is  
20      absorbed by the disposable chemical strip 83 which has been manufactured into the disposable 33. The strip is then read in place by a milliamp/or millivolt sensing electronics depending on the specific chemistry of the test strip. This reading is converted into a chemical concentration by the onboard electronics and displayed on the LCD on the side of the device.  
25      The stop and adjustment tabs 19 control the depth of penetration of the lancet 30 so that the optimal depth of penetration is reached for a particular sample site.

- 30      Figures 16 and 17 illustrate an integration of the minimally invasive sampling device with a chemical test measurement, such as for glucose, using a disposable piercing apparatus 33, a reusable sampling device 1, a disposable absorbent test strip 83 capable of providing semiquantitative colorimetric results.

The device is comprised of numerous components which will be more fully described below. The main body is 1 which supports the various mechanical and electrical components housed within the device.

The main body 1 comprises of an elongated hollow cylindrical tube with 5 openings at both ends. The lancing member 30 which is part of disposable 33 is capable of being retracted or deployed so that it can protrude beyond the end of the main body 1 is positioned at one end. The arming tabs 37 protrude from the sides of main body 1. The lancing member 30 is guarded by being withdrawn into the tube 35 which is part of the disposable 33. The tube 35 acts 10 as the lancing guide and lancet guard. The disposable 33 is attached to the main body 1 so that it is positioned at the appropriate location to guide the lancet and is held in place by the disposable clamp 3. The striker 39 is projected so as to drive the lancet into the patient 41 by the spring 43 and the arming plunger assembly 36. The arming plunger is locked in place by a cam 15 45 and trigger 47. A double stop return spring 49 is located and sized to return the lancet 30 back into the tube 35.

The double stop return springs 49 provide a mechanism after activation to pull the needle back out of the wound to permit blood 61 accumulation. When the skin is pierced the secondary springs 49 retract the needle from the 20 wound and initiate the stimulation ring 25 oscillation system to force blood flow to the wound. The cam 55 oscillates the oscillator ring 57 which transmits the motion to stimulation ring 25. The stimulator ring can oscillate in the preferred range of 1 to 5 mm. The frequency can vary from 20 to 200 cycles per minute in the preferred embodiment. The oscillation of the stimulator ring 25 is driven by the motor 51. The battery 56 provides energy to run the motor 51 which oscillates the stimulator ring 25 to pump the blood 61 from the surrounding capillaries in the skin into the wound. Each down stroke of the stimulator ring 25 compresses the stimulator spring 53 which provides the return motion for the stimulator ring 25. The disposable chemical strip 83 is then 25 lowered onto the blood bead using a secondary motion spring 74 that is released by a secondary motion trigger 75, and suction of the blood initiated. The blood 30

is absorbed by the disposable chemical strip 83. The strip is then removed and read by the patient.

The stop and adjustment tabs 19 control the depth of penetration of the lancet 30 so that the optimal depth of penetration is reached for a particular  
5 sample site.

Figure 18 illustrates an integration of the minimally invasive sampling device using a disposable piercing, stimulating and puncture depth adjustment apparatus 92. The device can assume any of the configurations described by this invention. This modification replaces items 19, 30, 72, 25, 3 on a typical  
10 reusable sampling device such as Figure 11. The disposable unit can incorporate a test strip, a sample container, an electrical sensing unit, or other testing or sampling component.

Figure 19A shows the concept of a dual alternating stimulation ring system. The secondary stimulation ring 120 alternates its position 180 degrees  
15 out of phase of stimulation ring 25. This creates a peristaltic pumping action on the capillaries adjacent to the wound. This device can be used with any embodiment to increase the blood flow. Link 121 connects the two rings with body 1. The peristaltic pumping results in squeezing the body fluid to the wound by massaging the fluid inward towards the wound.

20 Figure 19B shows the concept of concentric collapsing stimulation ring. In this embodiment the inner ring 25 contacts the skin after the outer ring 120. Spring 299 provides resistance and sequencing so that the outer ring 120 contacts the skin prior to inner ring 25. This squeezes the body fluid to the wound by massaging the fluid inward towards the wound.

25 In an alternate embodiment ring 25 can also function as the sample collection tube after lancing needle 16 is retracted.

In another alternate embodiment compressed gas pulses can be applied in the annular spaces between housing 1 and ring 120 and/or between ring 120 and ring 25 to massage the skin and stimulate blood flow. Such action by  
30 compressed gas pulses can be used instead of or in combination with the movement of ring 120 or other stimulation members.

Figure 20A illustrates a bell shape capillary tube 150 which is used to capture a sample of body fluid. The bell shape capillary is shaped to fit around the drop and it is drawn up the tube until it reaches the bulb 151. This assist in assuring that adequate sample 152 is drawn and the bulb 151 breaks the  
5 capillary action. The sample 152 is dispensed by compressing the bulb 151. The capillary can be heated to increase the draw of the capillary tube and the speed of the sample collection.

Figure 20B and 20C show an alternative method where the sample 152 is wicked up the tube 150 and the tube is inverted so that the sample can by  
10 transferred to a absorbent test pad 153.

Figure 20D shows a strait capillary 310 where the sample 152 is wicked up the tube 310 and is transferred to the absorbent test pad 153 by capillary action of the pad.

The tubes shown in 20A, 20B, 20C, and 20D can be modified with a  
15 surfactant to increase the ability to wick up the bodily fluid.

Figure 21 illustrates a device where the oscillation ring 130 is fixtured to disposable clamp 3 to oscillate the needle 33 to stimulate the wound and hold it open so that it does not close around the wound. In addition a heated ring 135 can be used to increase the capillary volume to stimulate blood flow.  
20

Figure 22A shows a multiple needle lancing device which is used to cause multiple wounds to increase sample size. The multiple needles are of sufficient size and length to minimize the pain sensation and still generate adequate sample size.

Figure 22B shows a broader single lancet which is used to cause multiple  
25 wounds to increase sample size.

Figure 22C and 22D shows a die cut sheet which has small multiple barbs formed in it which is used to cause multiple wounds to increase sample size. The multiple barbs are of sufficient size and length to minimize the pain sensation and still generate adequate sample size.  
30

The lancing device of Figures 22A through 22D can be used in the sampling devices disclosed herein.

We Claim:

1. A device for obtaining a sample of body fluid through the skin comprising:
  - a housing member suitable for use and adapted to contain a needle for piercing the skin;
  - 5 a spring member in the housing for urging the needle to protrude from the end of the housing sufficient to penetrate the skin;
  - a plunger member for retracting the needle against the spring tension and a trigger member to engage the plunger to hold the needle retracted until released by the trigger;
  - 10 a stop member to limit the depth of needle penetration of the skin when released by the trigger;
  - a sample container communicating with the needle for receiving the sample from the needle; and
- 15 a second spring for retracting the needle from the skin and a suction cam and plunger activated upon the retraction of the needle for drawing the sample of fluid which accumulates on the surface of the skin into the sample container.
2. A device according to claim 1 comprising a skin stimulation member for contacting and massaging the skin:
  - a skin stimulation member for contacting and massaging the skin;
  - 20 an oscillation system for oscillating the skin stimulation member; and
  - a spring and actuator member adapted for activating the oscillation system upon retraction of the needle from the skin.
- 25 3. A device according to claim 2 comprising:
  - an actuator to deploy the stimulation member in the down position before needle penetration of the skin for holding the skin taut and for providing accurate depth control of needle penetration.

4. A device according to claims 1, 2 or 3 comprising:  
an actuator system for cyclic movement of the needle in the vertical or horizontal direction while the needle is inserted into the skin.
  
5. A device for obtaining a sample of body fluid through the skin comprising:
  - a housing member adapted to contain a needle for piercing the skin;
  - a drive means in the housing for urging the needle to protrude from the end of the housing sufficient to penetrate the skin;
  - 10 a stop member to limit the depth of needle penetration into the skin by the device means;
  - a sample container communicating with the needle for receiving the sample from the needle;
  - means for retracting the needle from the skin; and
  - 15 means for drawing the sample of fluid which accumulates on the surface of the skin into the sample container upon needle retraction.
  
6. A device according to claim 5 further comprising a skin stimulation member for contacting and massaging the skin at the point of needle pierce;
  
- 20 a skin stimulation member for contacting and massaging the skin;  
an oscillation system for oscillating the skin stimulation member;  
and  
a spring and actuator member adapted for activating the oscillation system upon retraction of the needle from the skin.
  
- 25 7. A device according to claim 6 further comprising a spring and actuator member adapted for activating the oscillation system upon retraction of the needle from the skin.

8. A device for obtaining a sample of body fluid through the skin comprising:
  - a housing member suitable for hand held use and adapted to contain a member or system for piercing the skin;
  - 5 a sample collection tube positioned to collect a sample of fluid emerging from the pierced skin; and
  - an actuator for causing the member or system to pierce the skin.
9. A device according to claim 8 wherein the system for piercing the skin comprises laser system or a fluid under pressure directed to pierce the skin.
- 10 10. A device according to claim 8 wherein the member for piercing the skin comprises a needle positioned adjacent the end of the tube and driving member for urging the needle into the skin and a second member for retracting the needle from the skin.
11. A device according to claim 10 wherein the tube is a  
15 multichambered tube containing in one chamber a needle and adapted for receiving the sample in a second chamber.
12. A device according to claims 8, 9, 10 or 11 comprising a pump system for pulling the fluid sample into the tube.
13. A multichambered tube for use in a body fluid sampling device  
20 for obtaining a sample of fluid through the skin comprising:
  - one chamber in the tube containing a needle adapted for piercing the skin; and
  - a second chamber in the tube adapted for receiving a sample of fluid from the pierced skin.

14. A device for collecting a sample of body fluid from a wound in the skin comprising:

a housing member suitable for use containing a chamber for collecting a sample of fluid emerging from the wound; and

5 a skin stimulation member movably positioned at the end of the housing member for contacting a massaging the skin near the wound to stimulate the flow of fluid to and out of the wound.

15. A device according to claim 14 wherein a stimulation member is positioned between the chamber and the housing and is adapted to telescopically  
10 extend from the housing to contact the skin and pump the body fluid to the wound.

16. A device according to claim 15 wherein the stimulation member is adapted to increase the opening of the wound and enhance fluid flow from the wound.

15 17. A device according to claim 15 wherein the stimulation member is adapted to stroke the skin toward the wound to enhance fluid flow from the wound.

18. A device according to claim 2, 6 or 14 wherein the stimulation member comprises a polygon, square, circular or annular shape, a paddle or  
20 squeegee member, a system for employing a fluid under pressure to contact and stimulate the skin, or a fluid contained in a flexible membrane for contacting and stimulating the skin.

19. A needle for piercing the skin comprising a hollow tube having a pointed spade protrusion extending substantially longitudinally from a portion of  
25 one side of the end of the tube.

20. A needle according to claim 19 wherein the spade portion is angled toward the center line of the tube.
21. A needle having an angled or beveled tip for piercing the skin comprising a hollow tube wherein the longitudinal passageway in the tube is 5 eccentrically located in the tube.
22. A device for use in a body fluid sampling device for obtaining a sample through the skin comprising:
  - a standoff member adapted for contacting the skin;
  - 10 a sample collection tube positioned in the standoff member for receiving the fluid sample;
  - a lancet member movably positioned in the standoff member adjacent to the tube for piercing the skin; and
  - 15 electrodes positioned in the standoff member adapted for connection to a sensor to sense the presence of fluid within the standoff member.
23. The device of claim 22 further comprising electrodes positioned in the collection tube for connection to a sensor to sense the presence and amount of fluid within the collection tube.
24. A device according to claims 1, 5, 8, 13, 14, 20 or 22 further 20 comprising:
  - an integral test unit for testing the sample.
24. A device according to claim 23 wherein the test unit comprises a colorimetric test unit or an electrochemical test unit.
25. A device of claims 1, 5, 8, 13, 14, or 22 adapted to receive a test 25 device unit which absorbs the sample from the wound site.

26. A body fluid collection device comprising a capillary tube flared on one end for contacting the skin and having a suction member positioned on the opposite end.

27. A device according to claim 26 further comprising a test strip on 5 which the fluid sample is deposited from the capillary tube.

28. A device for use in a body fluid sampling device for obtaining a sample through the skin comprising:

an elongated holder member having a plurality of passageways extending longitudinally through the member; and

10 lancet members positioned in said passageways and adapted for creating a plurality of wounds in the skin when contacted with the skin.

29. A device for use in a body fluid sampling device for obtaining a sample through the skin comprising:

15 a plate member having a plurality of sharp protrusion extending from one side of the plate member adapted for creating a plurality of wounds in the skin when contacted with the skin.

30. A device according to claims 2, 6 or 14 wherein the stimulation member or system comprises a flat spiral spring, ultrasonic action, piezoelectric action, heating, friction or vibration.

20 31. A lancing device for piercing the skin comprising multiple lancing members formed from needles or barbs.

32. A method of collecting a sample of body fluid which includes piercing the skin;

mechanically stimulating the wound created by piercing the skin; collecting the sample which results from the stimulating; and dispensing the sample.

33. A device according to claim 4 wherein the activator system  
5 comprises ultrasonic, piezoelectric, mechanical or electrical action.

34. A device according to claims 1, 5, 8, 13, 14 or 22 further comprising a system for injecting a material into the skin.

35. A device according to claims 1, 5, 13, 14 or 22 further comprising suction means for pulling a sample into the needle, tube or chamber.

10 36. A device according to claims 1, 5, 8, 13, 25, 22, 28, 29 or 31 wherein the needle, the system for piercing the skin or lancet member is adapted to pierce the skin at an angle less than 90°.

37. A device according to claim 36 adapted to stimulate the skin prior to or during the peircing the skin.

15 38. A device according to claims 1, 5, 8, 13, 14, 22, 28, 29 or 31 wherein the portion of the device which pierces the skin and the portion of the device which collects or contains the sample are disposable units.

20 39. A device according to claims 1, 5, 8, 13, 14, 22, 28, 29 or 31 wherein the portion of the device which pierces the skin is adapted to oscillate while inserted into the skin which oscillation is by vertical, horizontal, rotation or cyclic movement.

40. A device according to claims 1, 5, 8, 13, 14 or 22 further comprising a system for imposing an electric potential across the skin from a

point distant from the wound in the skin to a point near or in the wound in the skin.

41. A device according to claims 1, 5, 8, 13, 14 or 22 comprising a system to measure the volume of the sample collected.

5 42. A device according to claim 41 wherein the measuring system is adapted to stop the sample collection at a predetermined volume of sample.

10 43. A device according to claims 1, 5, 8, 13, 14, 22 or 26 wherein the sample container or sample collection tube comprises a material having an affinity for the sample fluid sufficiently high to collect the fluid sample from the surface of the skin but sufficiently low to allow the fluid sample to wick from the container or tube when placed in contact with a test strip or device having an affinity for the fluid sample higher than that of the container or tube.

15 44. A method of collecting a sample of body fluid comprising:  
piercing the skin with a hypodermic needle;  
withdrawing the needle from the skin;  
massaging an area adjacent the wound; and  
collecting a sample of fluid from the surface of the skin into the hypodermic needle.

20 45. A method for collection a sample of a body fluid comprising:  
mechanically massaging a skin area;  
piercing the skin to create a wound;  
mechanically massaging a skin area adjacent the wound; and  
collecting a fluid sample from the wound or the surface of the skin.

25 46. A method according to claim 45 comprising inserting a device to pierce the skin and oscillating the device in the wound.

1/23

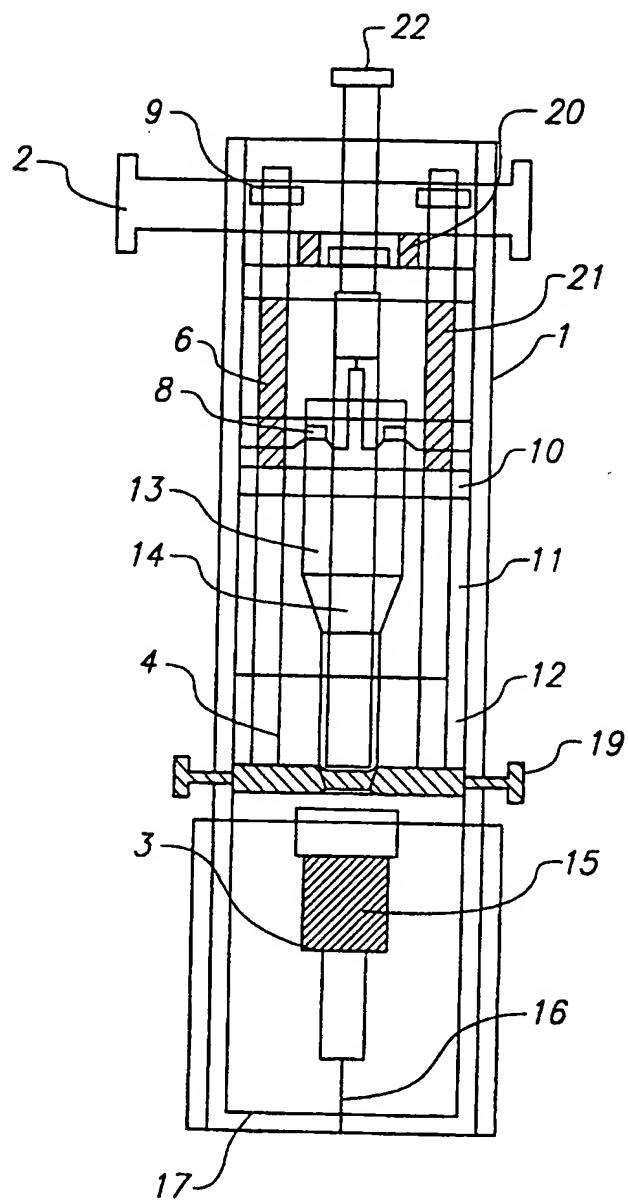


FIG. 1

2/23

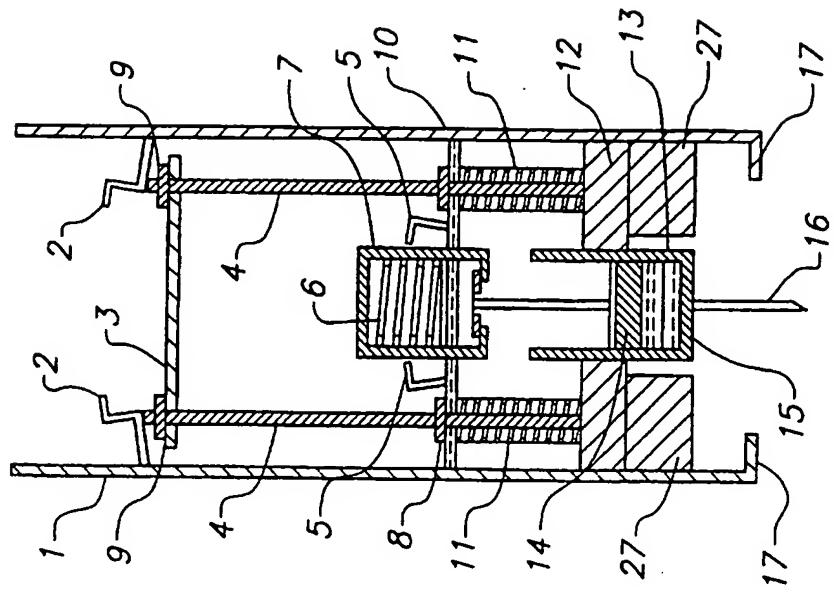


FIG. 2B

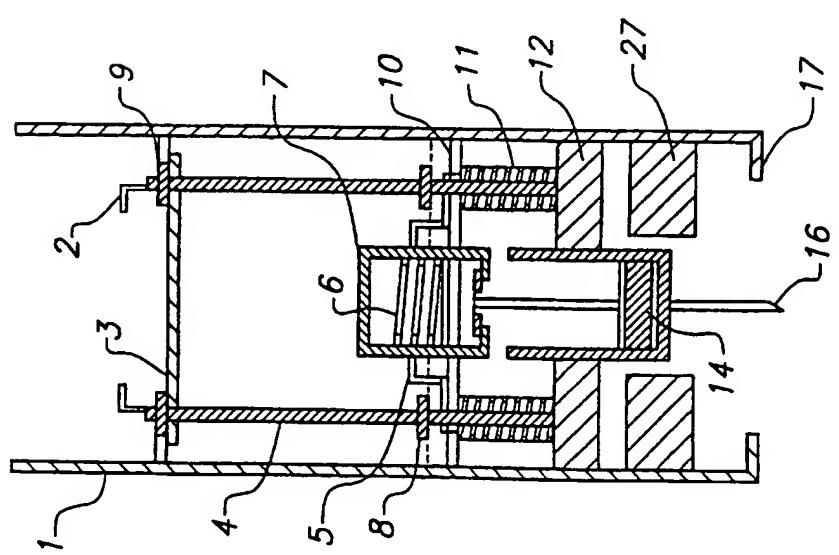


FIG. 2A

3/23

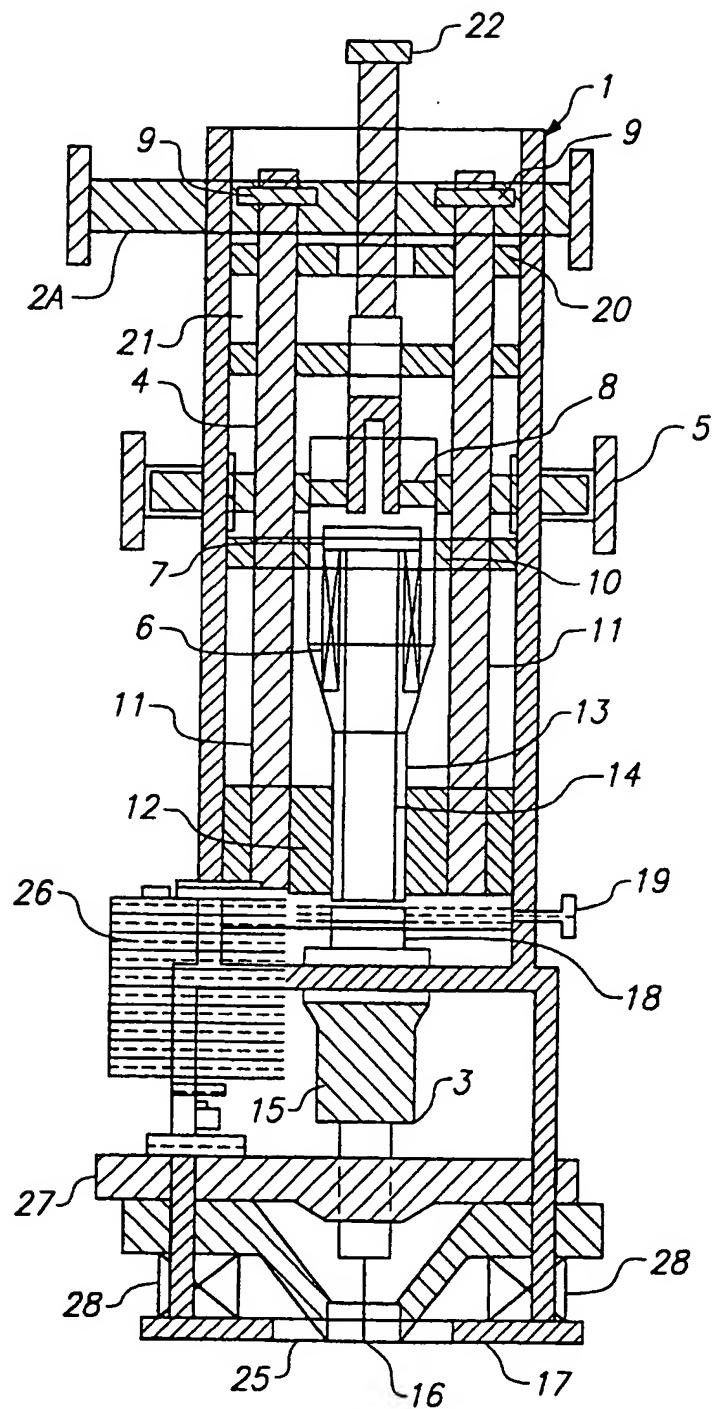


FIG. 3

4/23

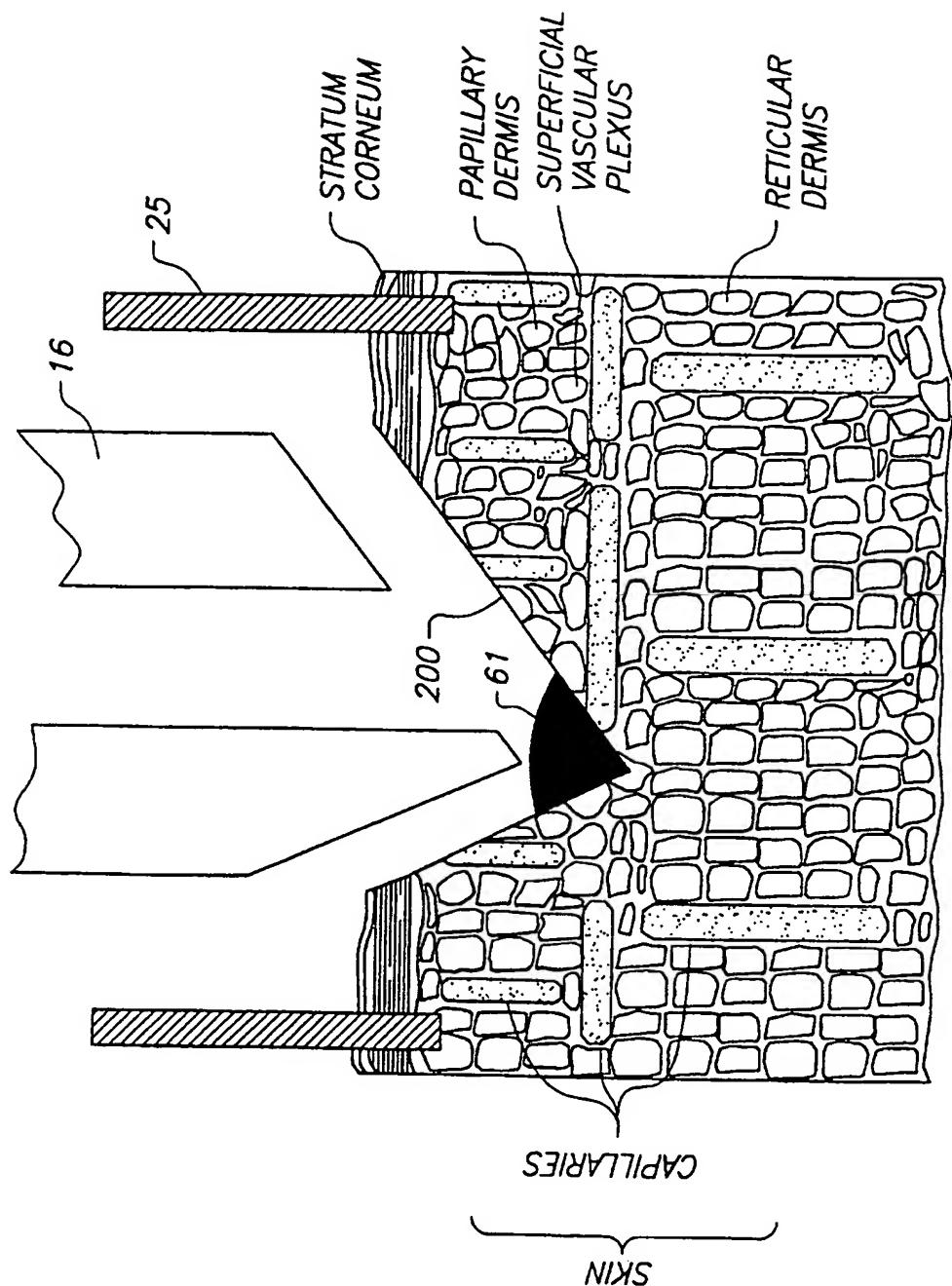


FIG. 4

5/23

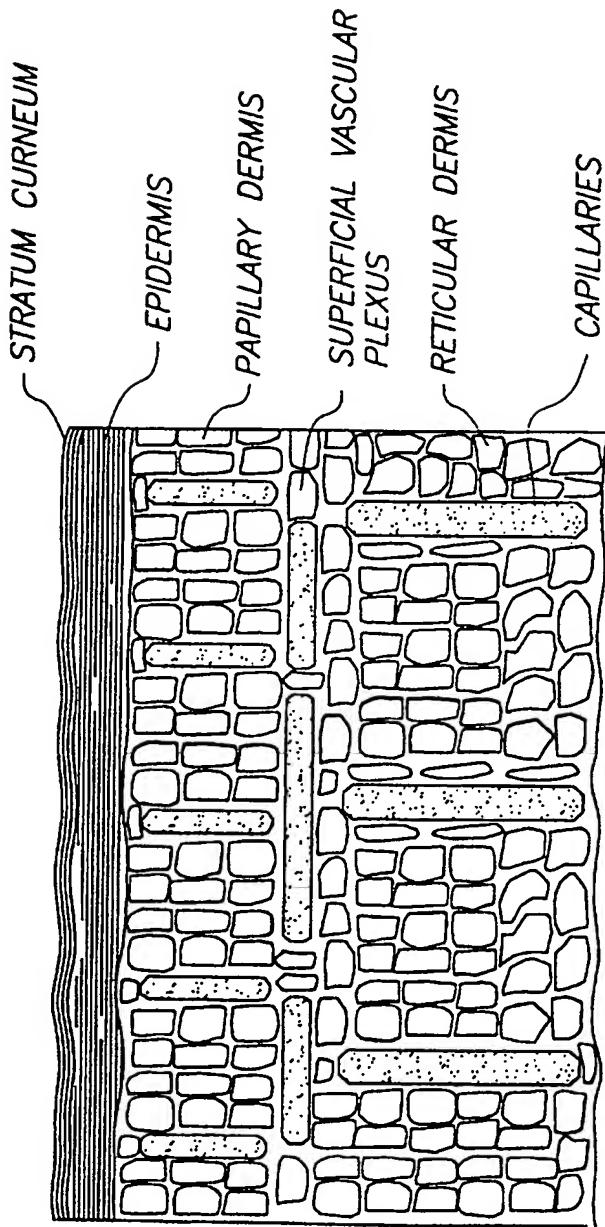
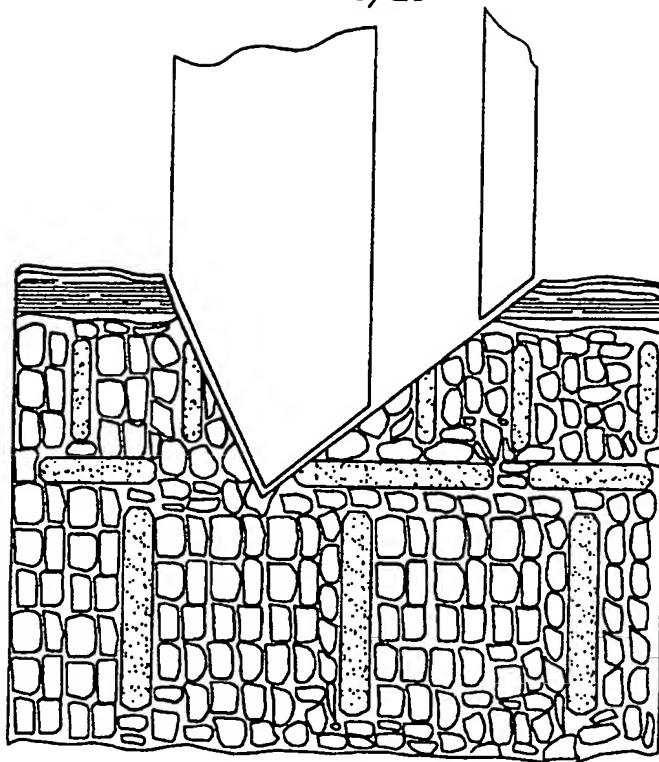
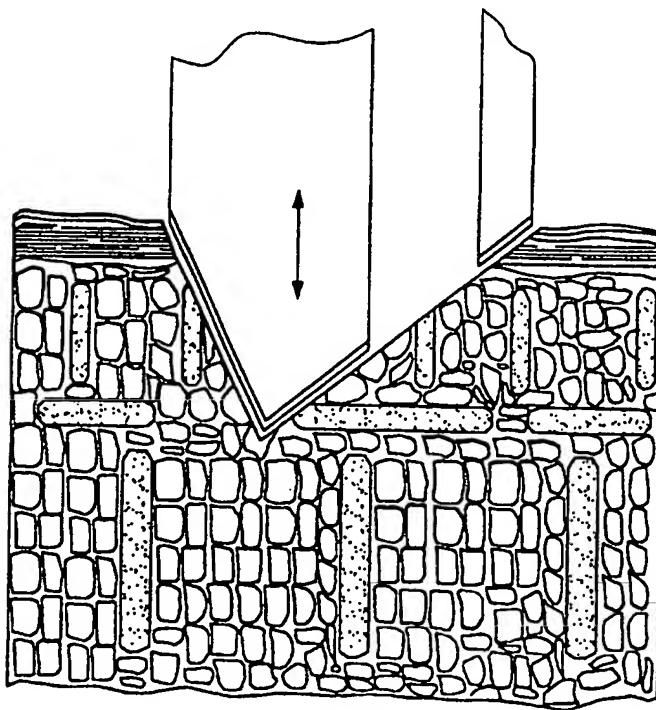


FIG. 4A

6/23

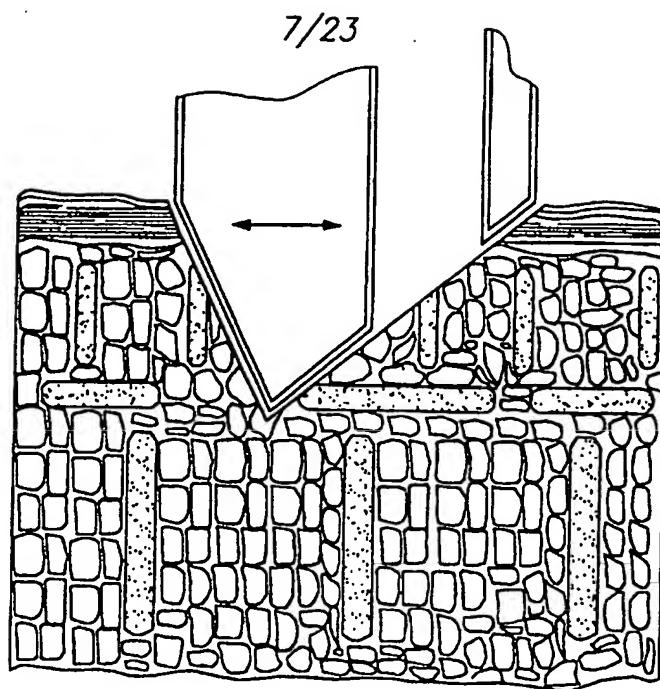


*FIG. 4B*

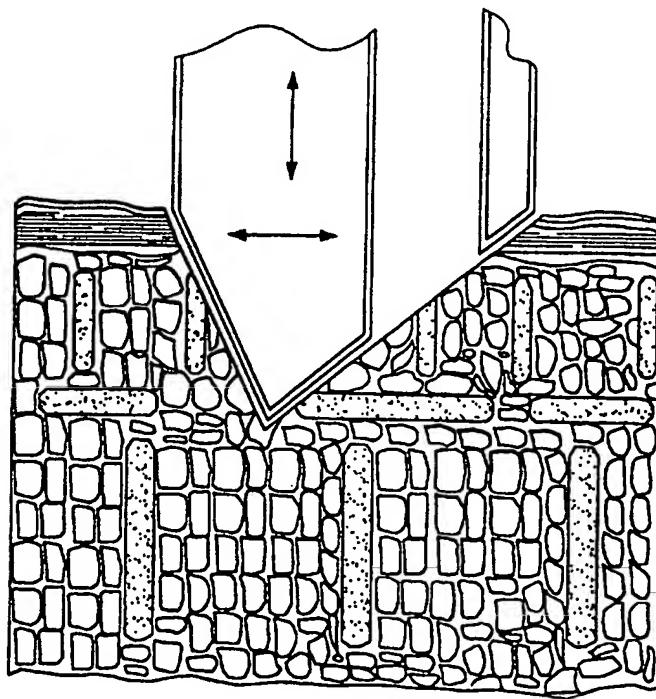


*FIG. 4C*

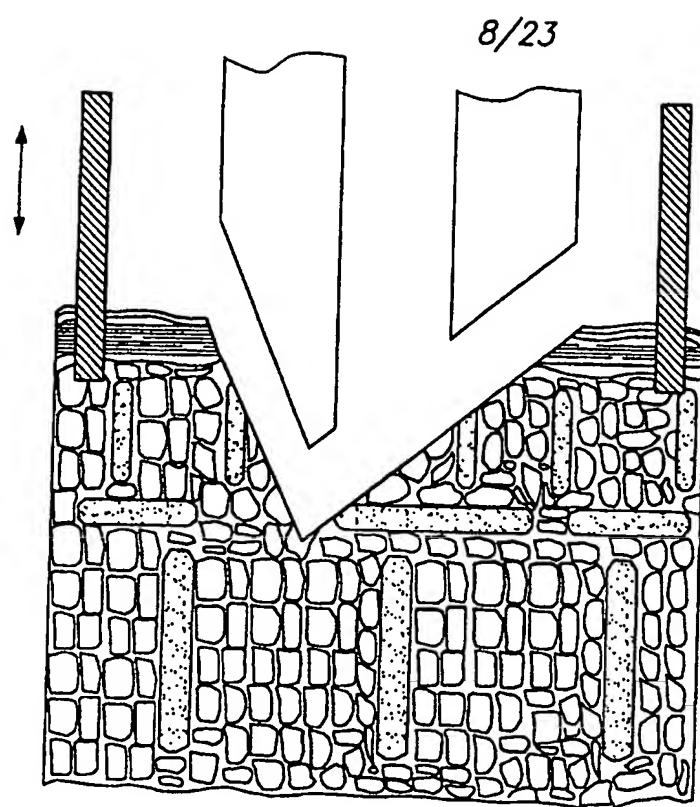
SUBSTITUTE SHEET (RULE 26)



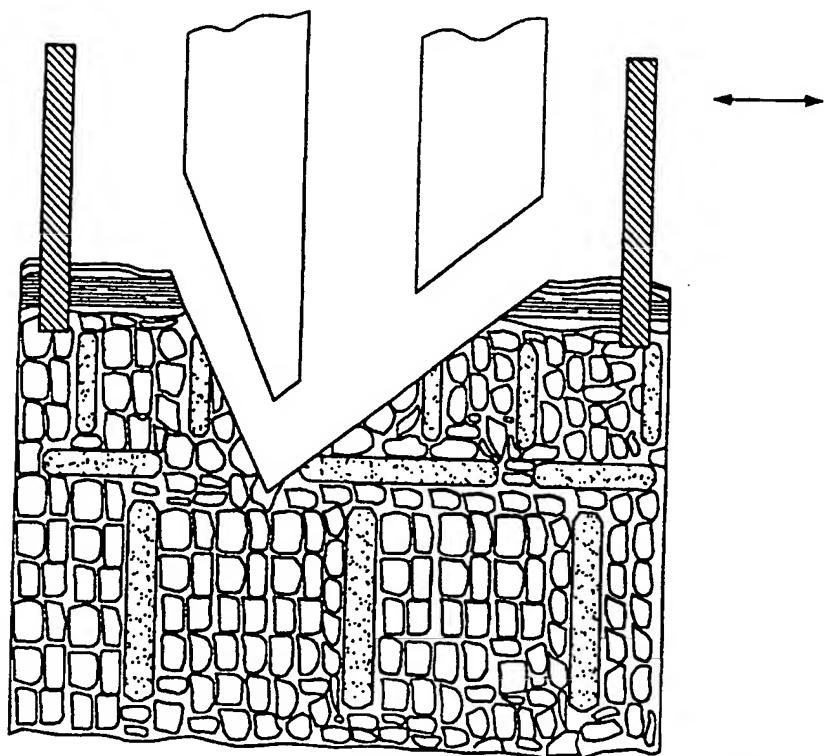
*FIG. 4D*



*FIG. 4E*



*FIG. 4F*



*FIG. 4G*

SUBSTITUTE SHEET (RULE 26)

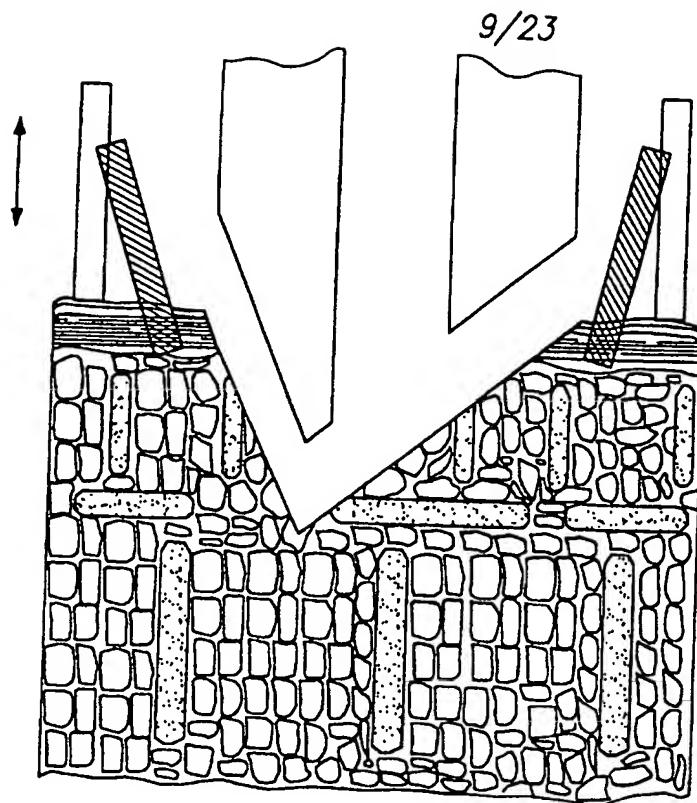


FIG. 4H

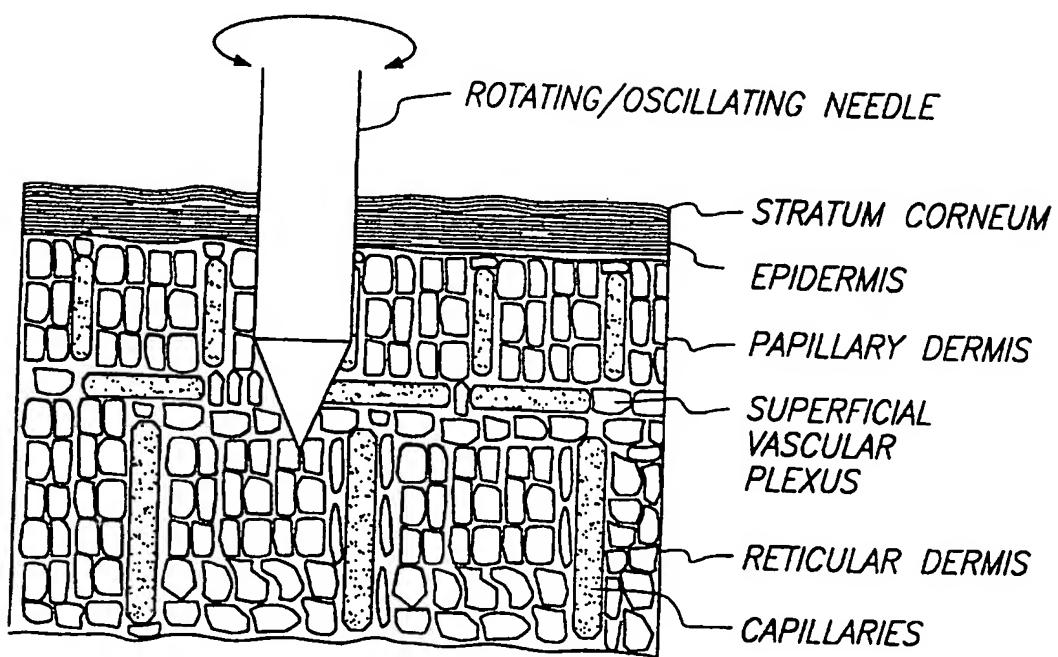


FIG. 4I

SUBSTITUTE SHEET (RULE 26)

10/23

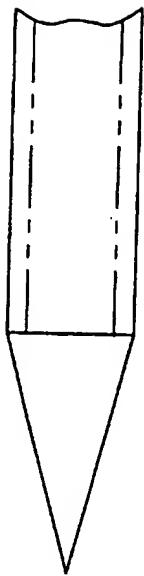


FIG. 5A

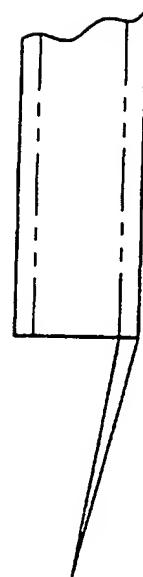


FIG. 5B

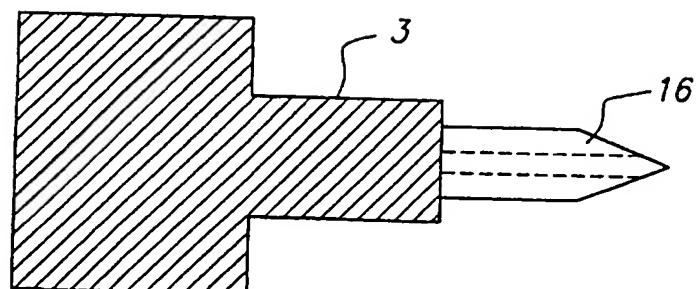


FIG. 6A

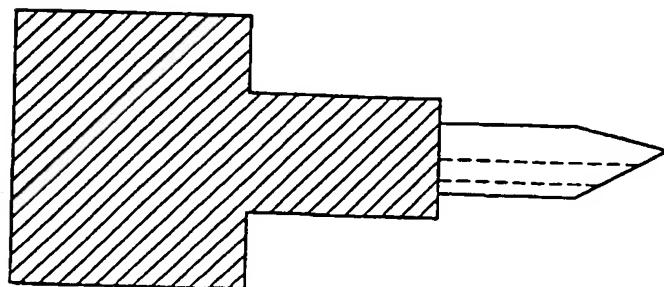


FIG. 6B

11/23

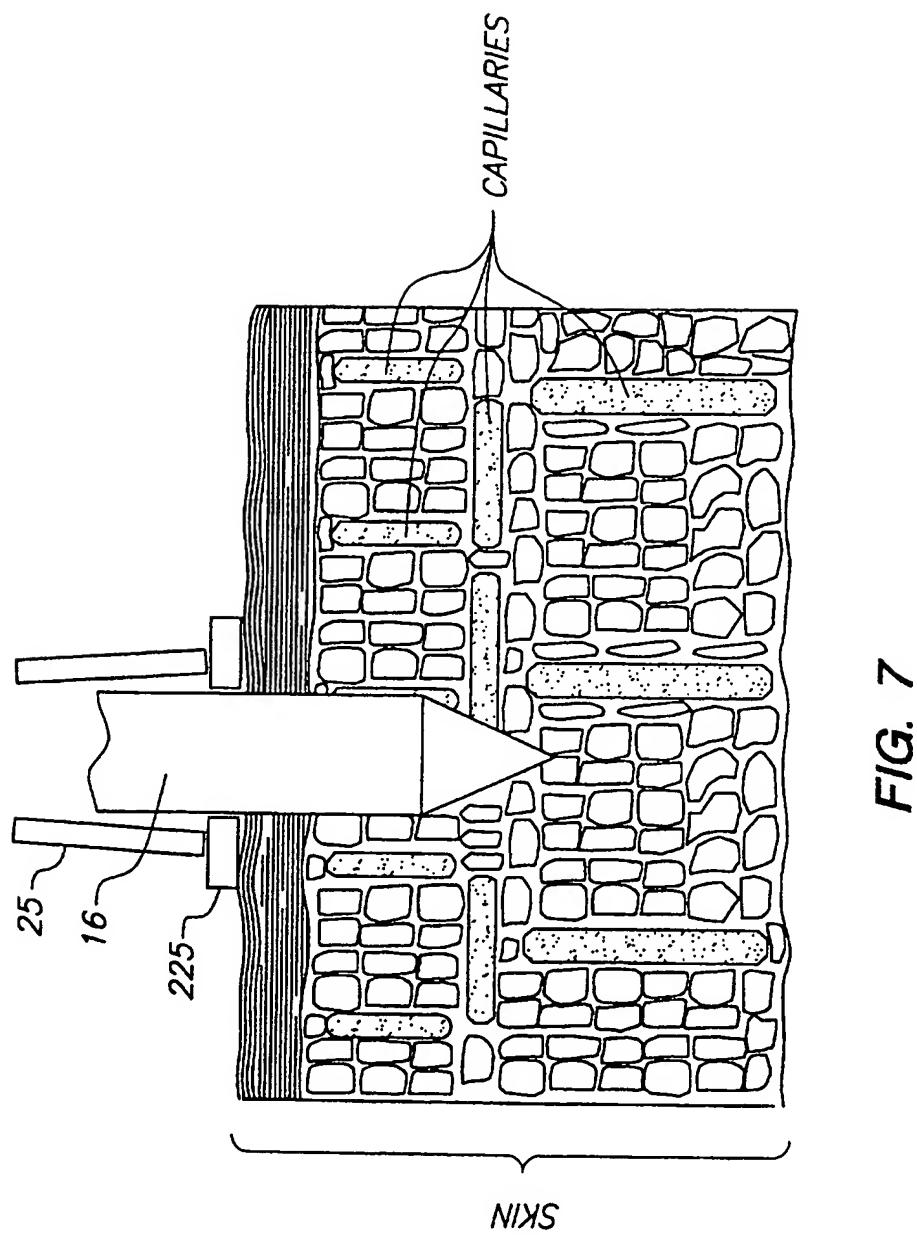
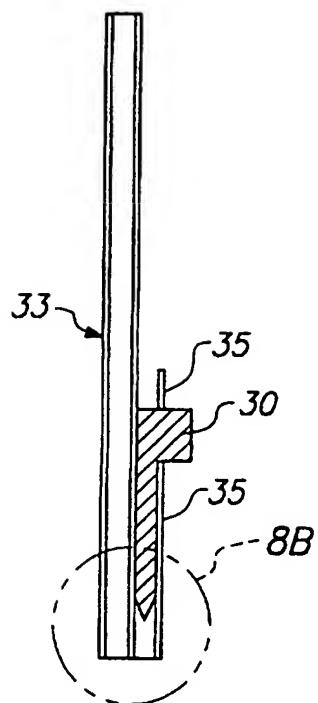
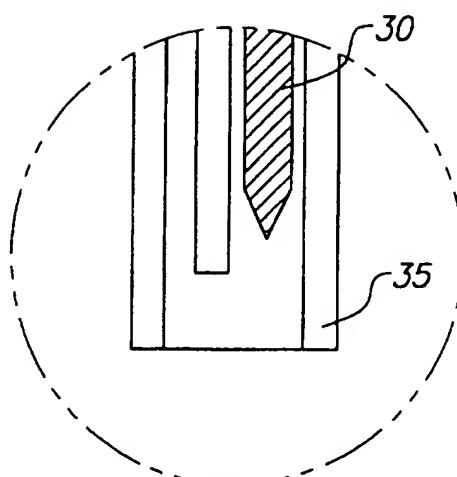
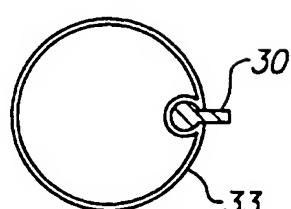
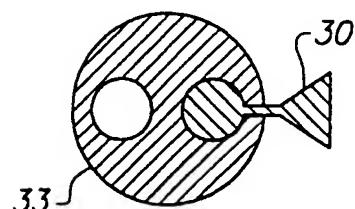
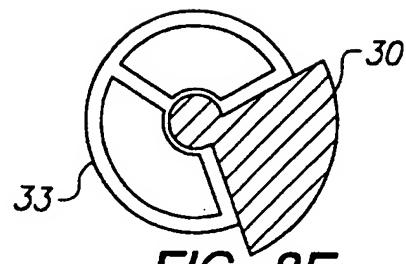
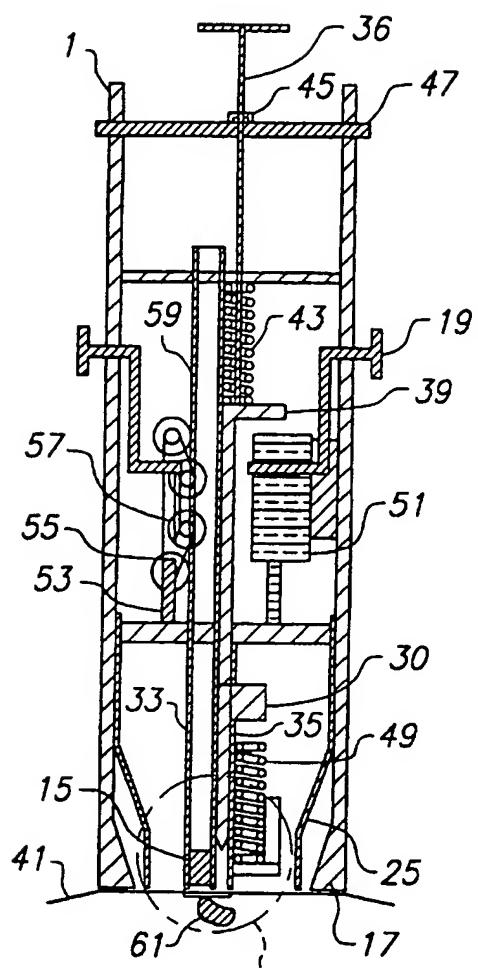
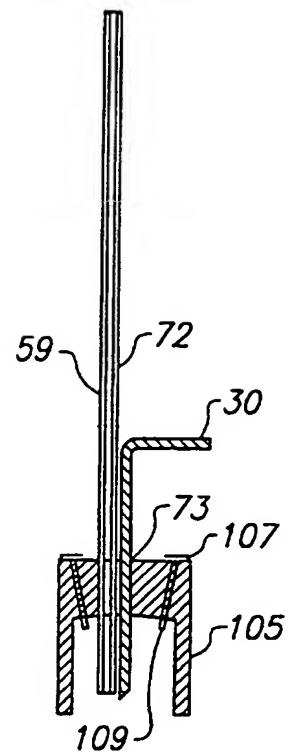
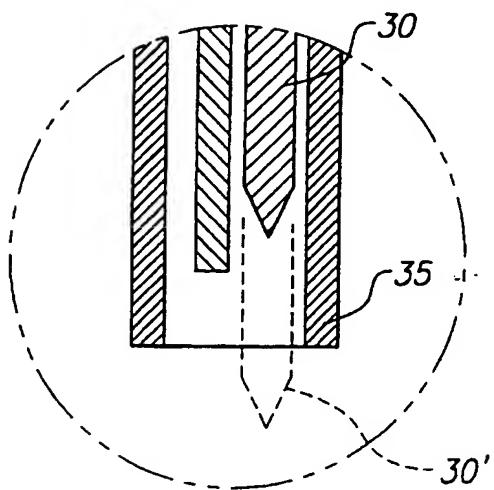


FIG. 7

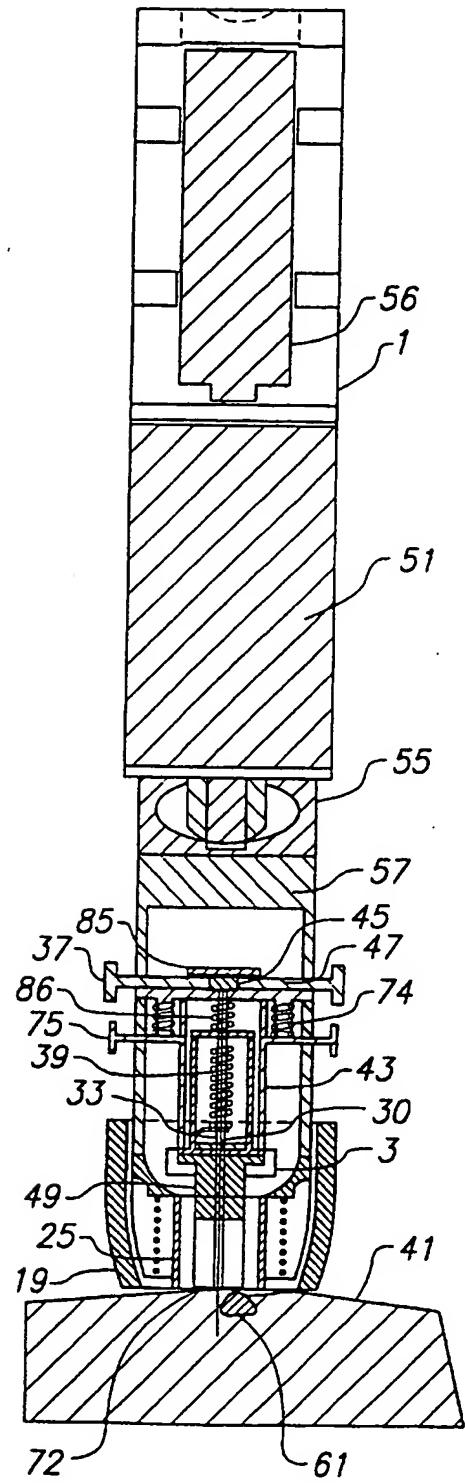
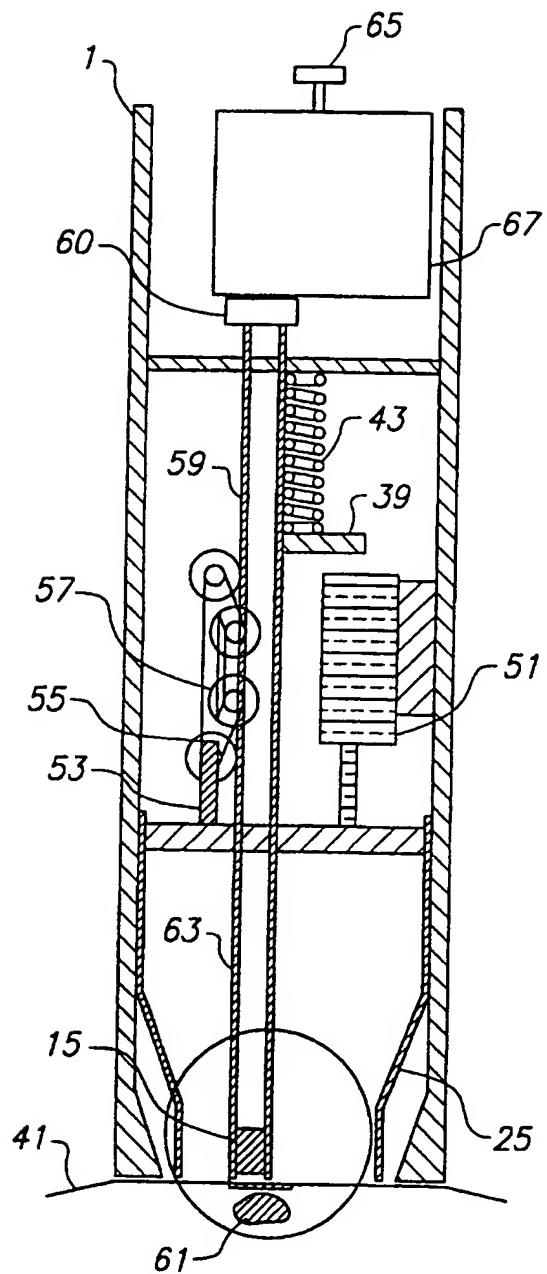
12/23

**FIG. 8A****FIG. 8B****FIG. 8C****FIG. 8D****FIG. 8E**

13/23

**FIG. 9A**

14/23



15/23

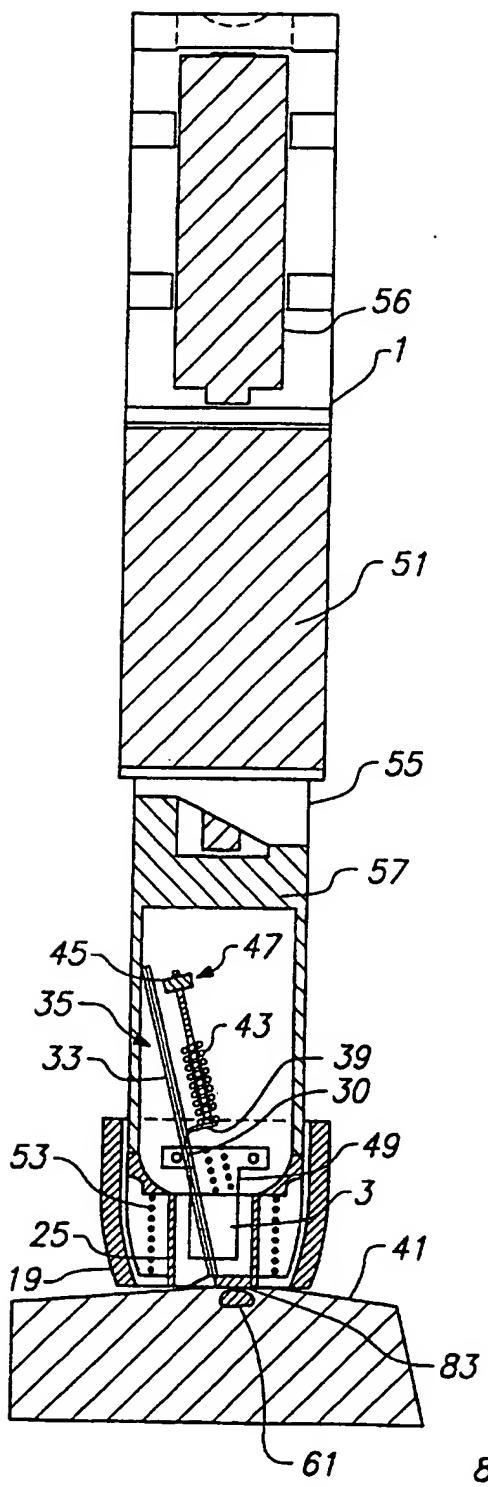


FIG. 12A

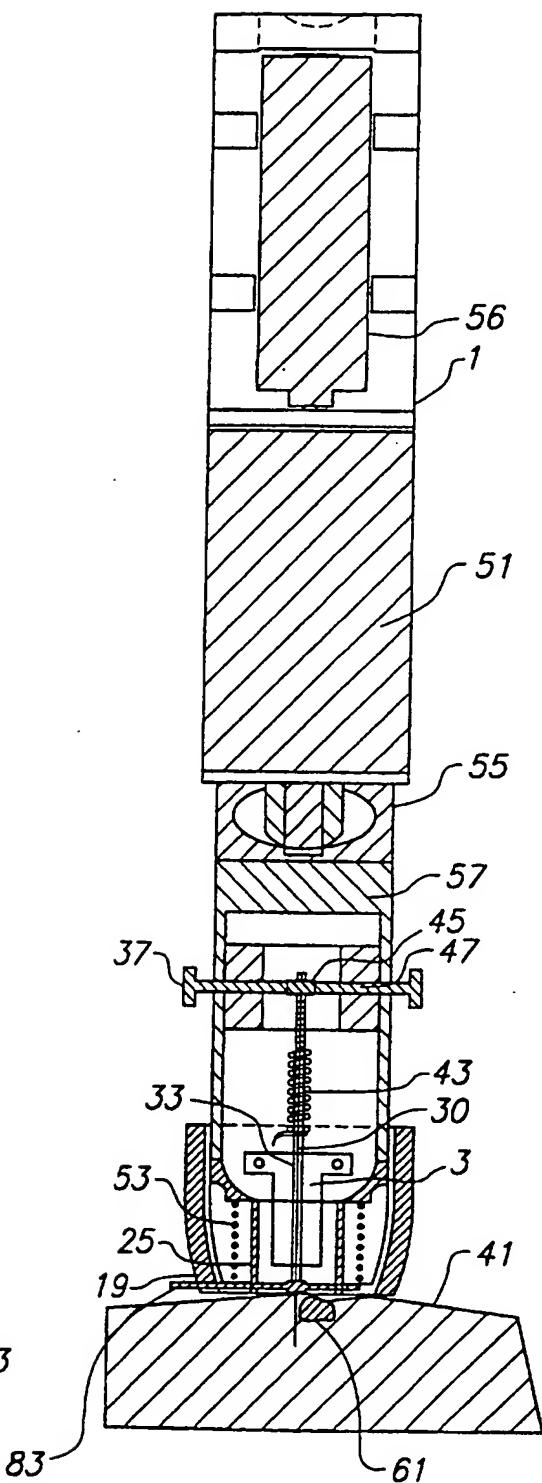


FIG. 12B

16/23

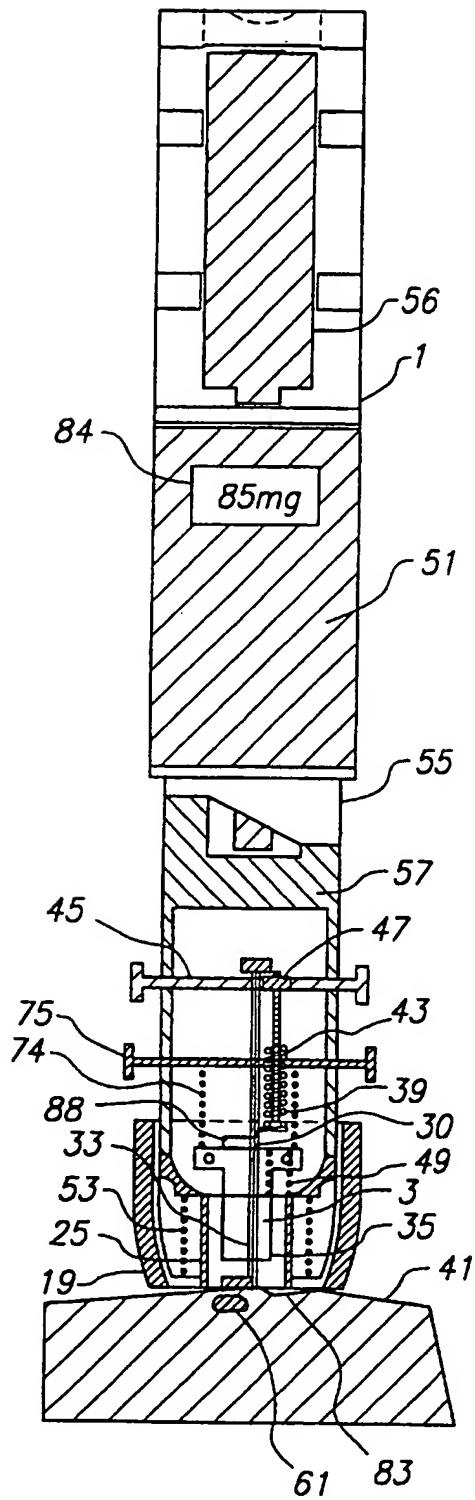


FIG. 13

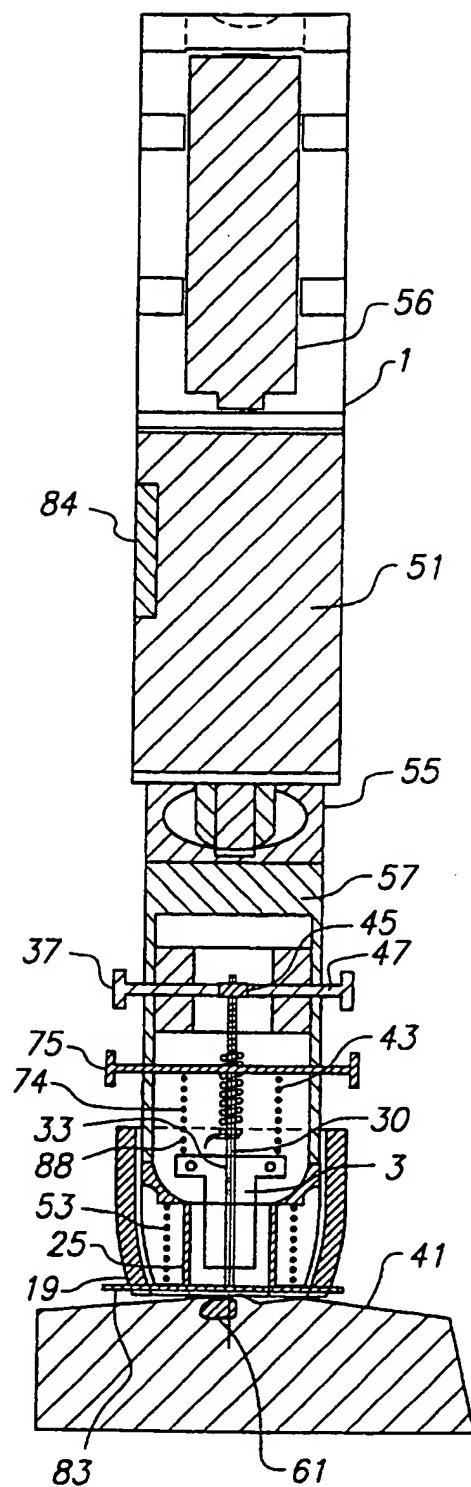


FIG. 14

17/23

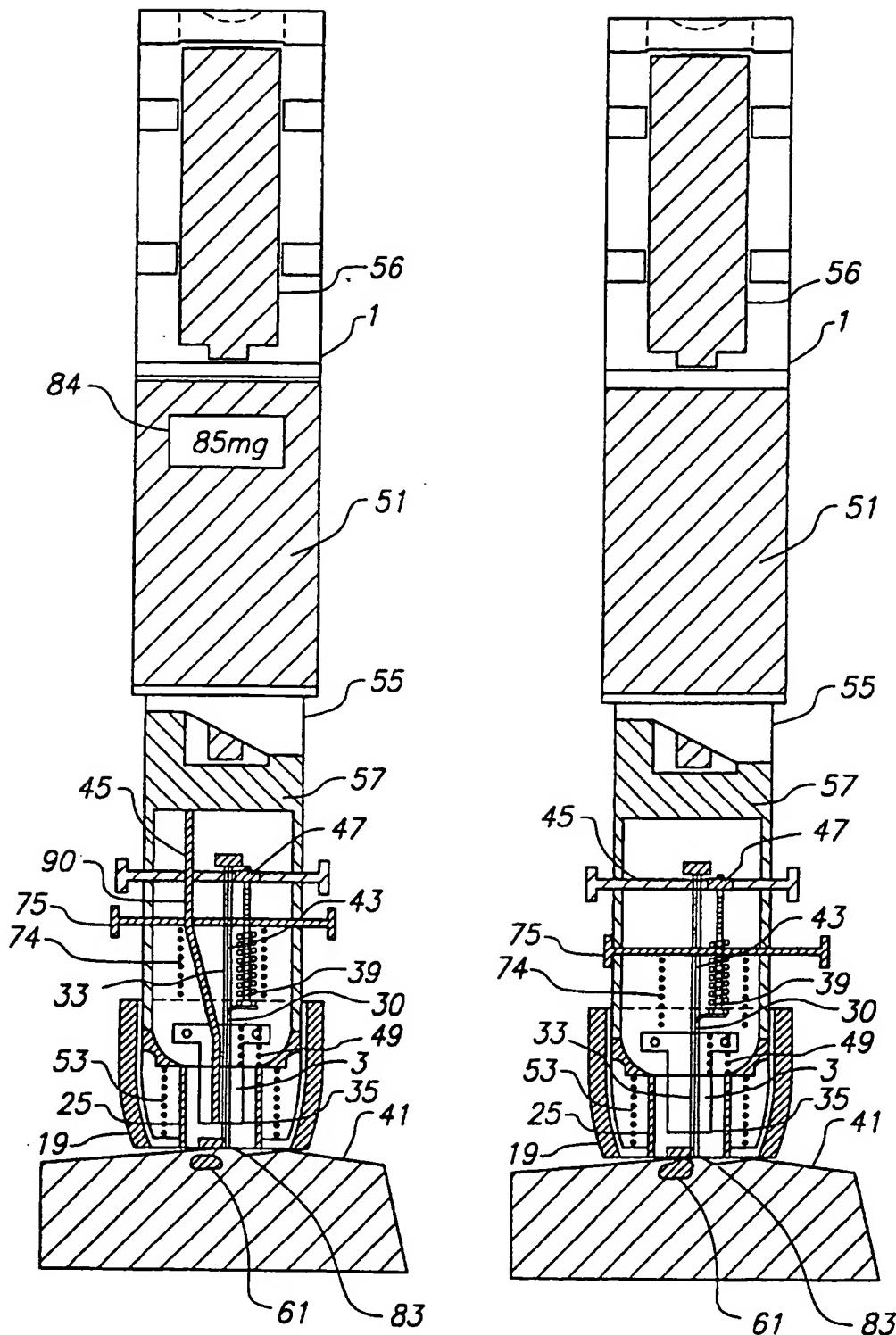


FIG. 15

FIG. 16

18/23

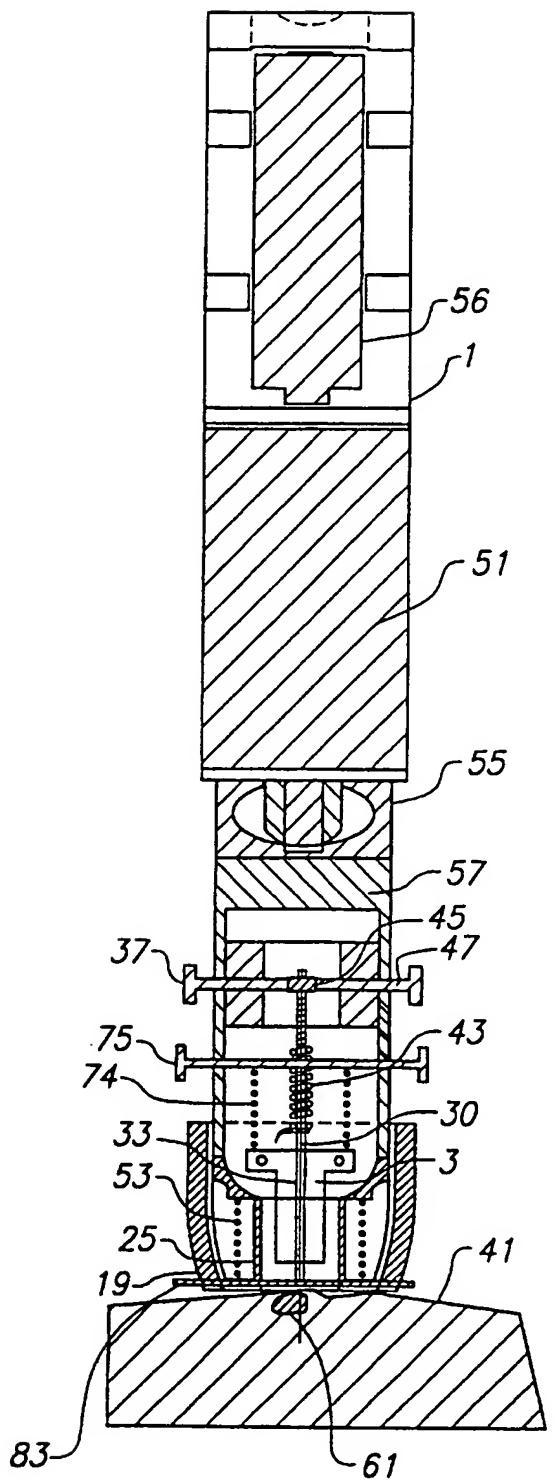


FIG. 17

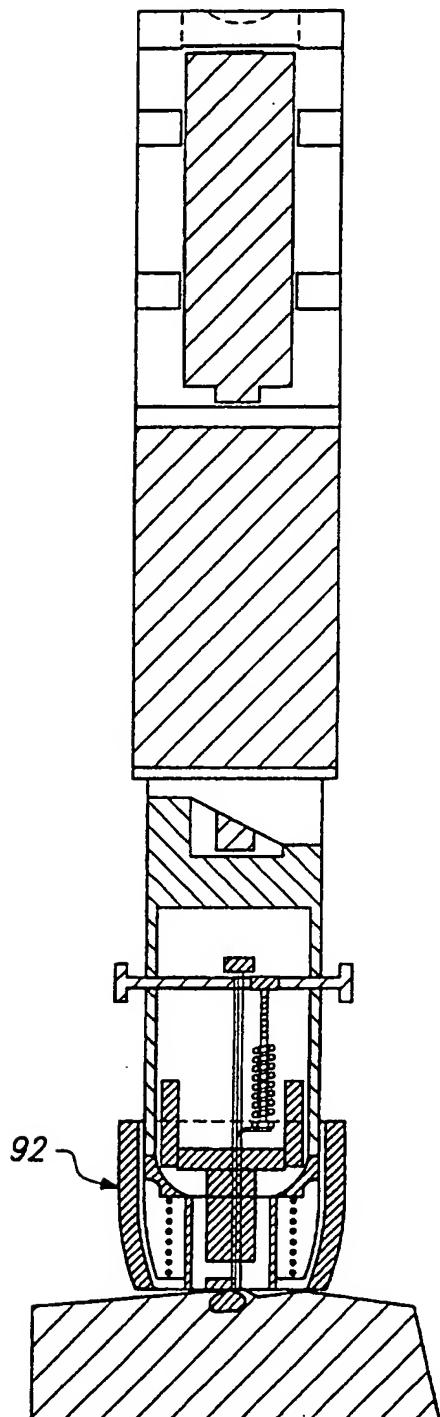


FIG. 18

19/23

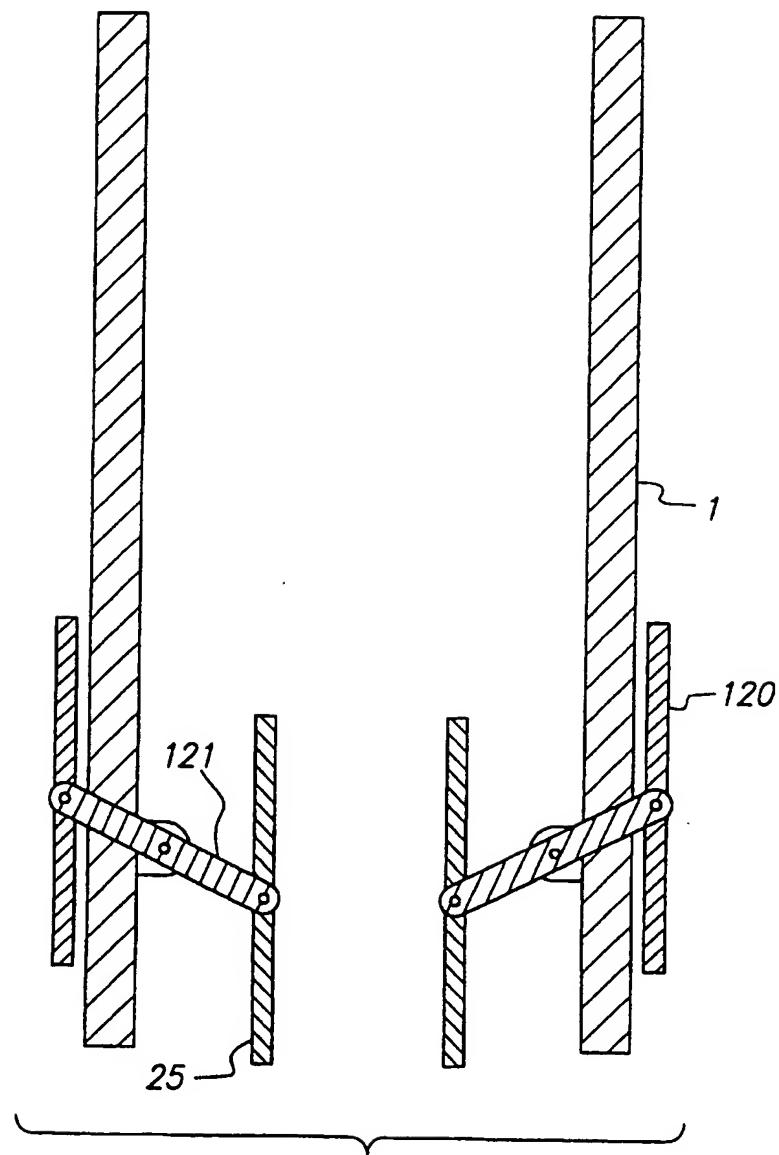
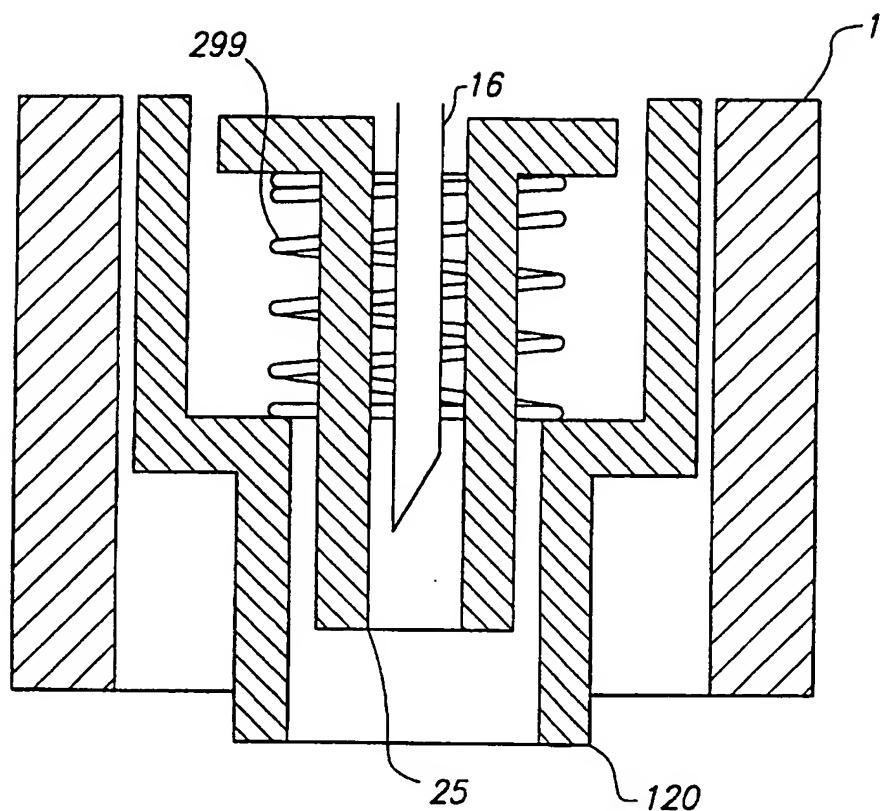


FIG. 19A

20/23

**FIG. 19B**

21/23

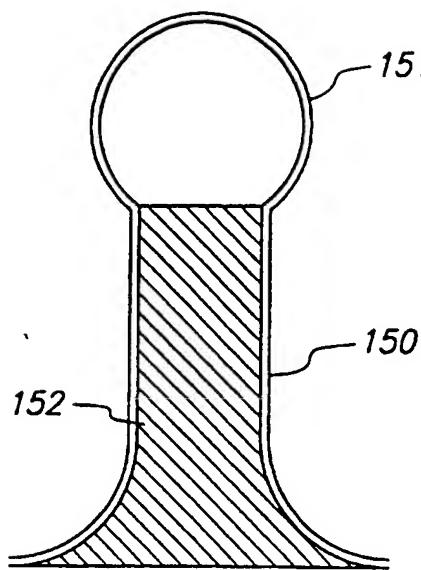


FIG. 20A

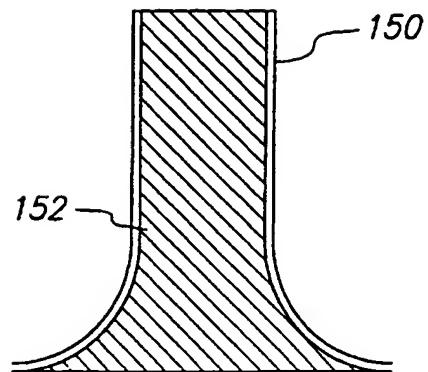


FIG. 20B

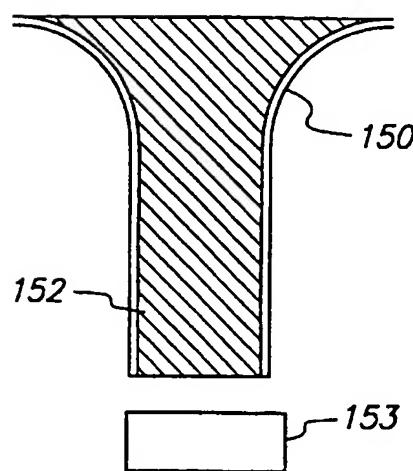


FIG. 20C

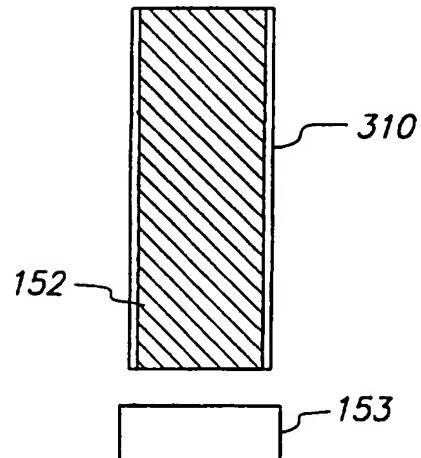


FIG. 20D

22/23

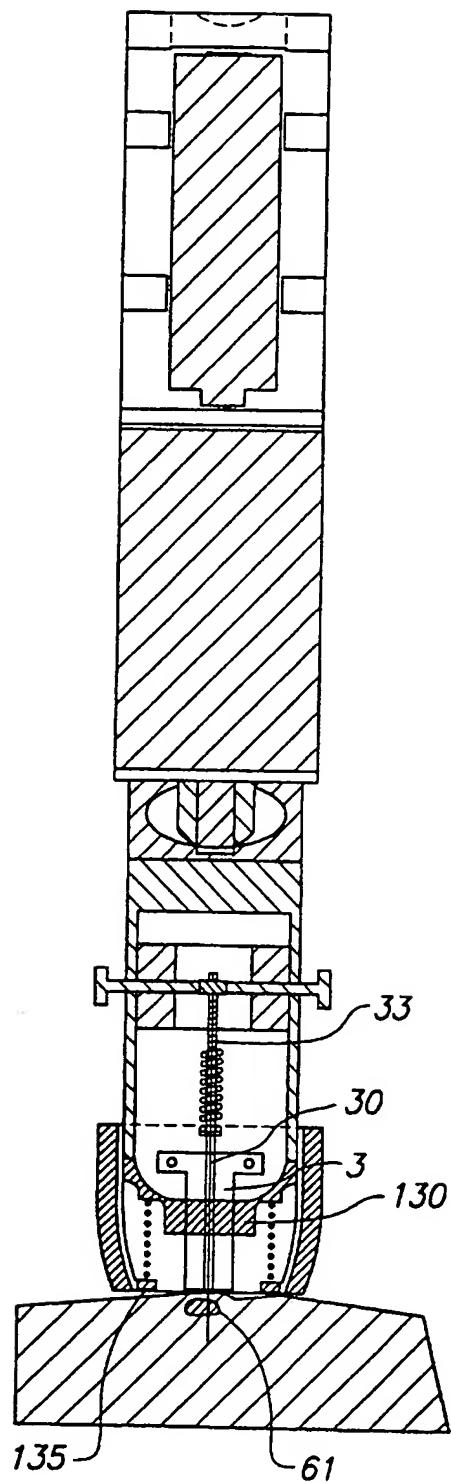


FIG. 21

23/23

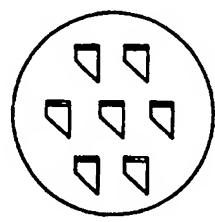
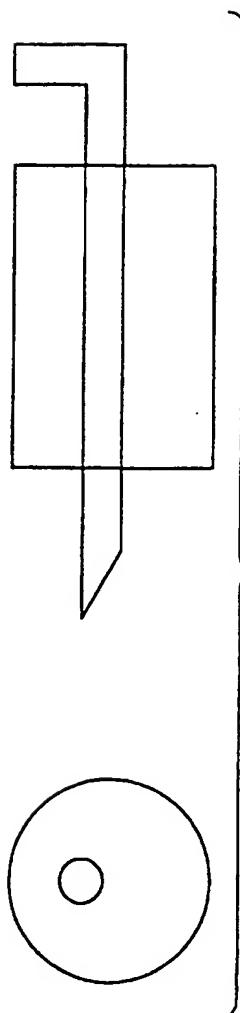
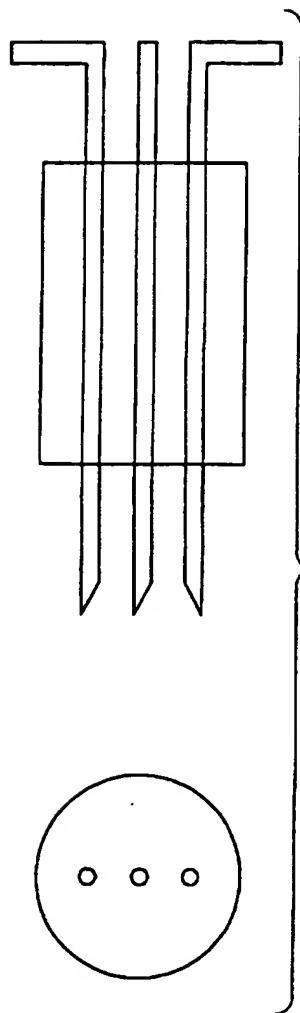


FIG. 22C

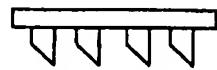


FIG. 22D

## INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/08762
---

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) :A61B 17/32

US CL :606/181

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/181

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,368,047 A (SUZUKI et al.) 29 November 1994, entire document.	1, 5, 8, 10, 12, 19-21, 41, 42
X	US 5,165,418 A (TANKOVICH) 24 November 1992, entire document.	8, 9
X	US 4,637,403 A (GARCIA et al.) 20 January 1987, entire document.	8, 23-25
X	US 4,994,073 A (GREEN) 19 February 1991, entire document.	28, 29, 31
X	US 4,627,445 A (GARCIA et al.) 09 December 1986, entire document.	14, 30, 32, 38, 41, 42.
X	US 4,360,016 A (SARRINE) 23 November 1982, entire document.	10, 11, 13

<input checked="" type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
-------------------------------------	--	--------------------------	--------------------------

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*'A'		document defining the general state of the art which is not considered to be of particular relevance
*'E'		earlier document published on or after the international filing date
*'L'		document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
*'O'		document referring to an oral disclosure, use, exhibition or other source
*'P'		document published prior to the international filing date but later than the priority date claimed
"X"		document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y"		document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"Z"		document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 AUGUST 1997	12 SEP 1997
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>Diane Smith</i> TINA T. D. PHAM
Faxsimile No. (703) 305-3230	Telephone No. (703) 308-0824

## INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/08762
---

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,687,000 A (EISENHARDT et al.) 18 August 1987, entire document.	8, 36